AN EXPERIMENTAL RESEARCH

UPON THE ABSORPTION OF PHENOL BY THE SKIN.

Being a Thesis for the Degree of M.D.,
Edinburgh University.

by

C A R L H. K R U G E R ,

M.B., C.M. (Edin.Univ.) 1896; F.R.C.S.E., 1898.

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TO

MY BELOVED MOTHER

I DEDICATE THIS THESIS.

INTRODUCTION.

It sometimes happens that in the course of his practice the Medical Practitioner is led to take an unwonted interest in a particular department of his profession, by some peculiar experience which he has met with. This may have been of a pleasurable kind - he may have had great success in his method of treating some disease, and by this means attracted the admiring notice both of his professional brethren, and of the public. Or, on the other hand, this experience may have been of an opposite character; he may have found himself in the painful position of seeing his treatment, instead of benefiting his patient and restoring him to health, have the effect of inflicting serious injury upon him, and even of bringing him to an untimely end. It is possible, also, that this may have resulted from no want of care or attention with which he could be justly charged, but solely from some defect in the state of Medical Science in regard to the particular subject with which he was concerned.

I regret to have to confess that a short time since I found myself in the last mentioned position.

I was so unfortunate as to see a child under my care in the Royal Infirmary, Edinburgh, die from the toxic effects of the absorption of Carbolic Acid applied to the skin in the ordinary way in the form of a poultice, for the purpose of disinfection previous to operation. Some very eminent surgeons have had experiences almost equally unfortunate, although, it may be, not ending fatally, e.g. amongst others those referred to by Lucas and Lane (Lancet I, 1895, p.1361 also II, 1897, p.537) of coma in 3 cases, 2 of them being infants 3 and 6½ years of age, and the third a young adult male of 15 years of age, by the external application of Carbolic Acid compresses of the strength of 1 in 20 of water. Langenbuch also (Berlin Klin: Wochenschr. Bd. 28, 1878, S.412.) met with the death of a child aged 5 years, after operation; but although in his case there was a linear incision, the absorption might be, for all practical purposes, considered as having taken place from an unabraded skin. In addition, we have the numerous poisonings by means of Carbolic Acid referred to by Billroth (Chir.Klin.Wien. 1879, S.39.) and by Falkson (Arch. fur Klin.Chir., Bd.26, 1881, S.204) as having resulted from the treatment of wounds by Lister's method.

Untoward events such as these have caused many to lose confidence in Carbolic Acid as a safe application for the purification of the skin, however much they approved of it as an effective antiseptic. Many opinions were entertained as to the real cause of these misadventures. Often the evil effects were attributed not to the phenol itself, but to impurities in it. Or again, the covering of too extensive a skin surface, or the possession of too large a quantity of Phenol in the poultice have each been imagined to be a source of the mischief. These diversities of opinion show the state of uncertainty in which this subject of the absorption of Phenol by the skin at present rests.

It occurred to me, therefore, that if exact and precise information could be attained with respect to the amount of the substance passing through the skin and affecting the constitution, and also to what extent injurious effects are attributable to impurities known to be often present, we should no longer be working in the dark, as is certainly to a great extent the case at present, when using this antiseptic.

It has been said that science is measurement, and many departments of Medicine cannot as yet be

dealt with by mathematical methods, as some expect will be the case some time in the future, yet the investigation I have undertaken can in its results be exhibited in precise figures. To remove this subject therefore from the region of doubt and uncertainty, and to place it on a solid basis of ascertained fact, would be a decided gain to medical science.

From one point of view the work which I have undertaken confines itself to very narrow and well defined limits, namely to ascertain what amount of Carbolic Acid is excreted in the urine when a poultice of a given strength of Carbolic Acid solution is applied to a given surface of skin for a given length of time and under certain conditions, as to the state of the skin and the amount of impurities present. But the subject gains in importance from the extensive use of this disinfectant and antiseptic in the present day; it would be difficult to indeed to name any agency which the surgeon finds it necessary to make use of more frequently.

And this matter has relations not only to the patient, but must be considered also as respects the operating surgeon and his assistants, who have continually to disinfect their hands and arms. The

quantity passing into the system by this means probably produces effects which are sometimes overlooked.

When we think of the lengthened time during which Carbolic Acid has been in use - from the inauguration of the new era of antiseptic surgery by Professor Lister in 1867 to the present - it is remarkable how little attention has been given to the absorption of Phenol when applied externally, and how little is known regarding it. Somehow or other this matter seems to have escaped the notice of medical men; they have been content with attending to the external antiseptic effect without paying much heed to the further process of absorption, and its effects, when in excess, upon the constitution.

That the subject deserves more attention, than has hitherto been bestowed upon it, is manifest when we consider that not only serious injury, but even death, as has already been noticed, has, in not a few instances, resulted from the external application of Phenol. The particulars of the case which so strongly as well as painfully impressed me, and which was the means of leading me to make the absorption of Carbolic Acid from the unabraded skin the subject of my thesis are as follows:-

F.W., a male suckling, 3 months of age, suffering from congenital double Talipes-Equino-Varus, was admitted on Nov. 15th, 1897 to Wards 15 & 16 in the Edinburgh Royal Infirmary, under my care while House Surgeon to Mr. Cotterill. The child being exceptionally healthy, strong and sturdy, and rather more developed than babies usually are at that age, it was decided not to delay operation, since the deformity was rather marked and unfit for palliative treatment. So at about 1 p.m. on the afternoon of Monday, Nov., 22nd, the skin of his feet and legs were prepared for operation by being washed up with soap and hot water & then with Ether, then a poultice of Bi-carbonate of Soda was applied for about 4 hours. Upon removal of this, a poultice of Carbolic Acid of the strength of 1 in 60 was applied to both feet and both legs extending to a point just below the knees. This was removed at 9 p.m., having been on for about 4 hours, and then a weak Boracic Acid poultice was substituted overnight. As it is customary in these wards for patients to have a renewal of dressing immediately preceding the operation, the child's limbs were again washed up at about 9.30 a.m. on Tuesday morning and a fresh weak compress of Carbolic Acid of the strength of about 1 in 60 or 1 in 70 was again applied as before.

Owing to some pressure of work the child was not operated upon, and owing to the charge nurse having been busy in the operating theatre the poultice was not removed until about 1.30 p.m. the same afternoon, or about 4 hours after its application, when the attention of the nurse, who had by that time returned to the ward, was drawn to the baby as he lay in his cot giving some "peculiar, catching, choky cries", and "looked funny", she said. "She called the mother to see what was the matter with the child; she at once removed the poultices, washed the legs and took the child to the fireside, but did so merely to pacify the child. The child, usually very lively, looked very dull and depressed and continued to give these peculiar cries." Not improving, but, on the contrary, gradually getting worse, I was sent for at about 6.45p.m. 5¼ hours since the onset of the symptoms, and saw him then for the first time. Not having had an experience of such a nature before, and not expecting Carbolic Acid to be at the bottom of all the mischief, and judging from the rapid abdominal breathing and feeble pulse, it then appeared to me as if he had Pneumonia; but on finding no positive signs and not being able to satisfy myself as to the nature of the

condition, I asked my friend, Dr. Harvey, to see the infant. He too expressed a negative opinion but suggested that a hot bath and hot bottles, as well as some stimulants, were indicated. These were accordingly administered. I saw the child again at 8 p.m., six and a half hours after the onset, with more pronounced symptoms. He was semi-comatose, very pale and perspired profusely, especially about the head, with shallow but rapid abdominal breathing, 67 per minute, and with hardly any chest movements; the pupils were contracted, the eyes staring and turned up; and he took no notice of anything but lay listless in his mother's lap and looked very ill. On examining the chest again I could make out no abnormal signs except a few râles and rhonchi posteriorly. The abdomen, although slightly distended, was quite supple and lax. Some spasmodic convulsive twitchings occurred in the hands and arms, but the legs just dropped when they were lifted. His temperature was 102°F., the pulse rate was too rapid to be counted, and the pulse was very weak in force. From the above symptoms and by a dark stain noticed on his napkin, I at once suspected Carbolic Acid poisoning. More hot blankets were wrapped round him, Sodium and Magnesium

Sulphates and whisky were administered; and about 9 p.m. (8½ hours after) owing to the pulse being hardly perceptible, I made a hypodermic injection of Strychnine. But as the child, who had previously not been sick, vomited up everything again that was given by the mouth, very little beyond a little whisky and sulphates per rectum, could be administered. In the meantime I asked the nurse to try and collect me a specimen of his urine. At 12 p.m. (10½ hours after) his temperature was 101°F., the pulse was running and very feeble. Up to this time the nurse had been able to collect only a ¼ test tube of perfectly black urine; and from the time of the onset of the symptoms until death this quantity plus a few drops on his napkin seems to have been the only urine passed. My diagnosis of Carbolic Acid poisoning was thus confirmed. In spite of treatment the symptoms progressed, the breathing became more rapid, and very loud, the pulse feebler and hardly perceptible. I administered another hypodermic injection of Strychnine at 1 a.m. The child afterwards became perfectly comatose, and died at about 5 a.m., On Wednesday morning, Nov.24th, within 15½ hours from the time of the onset of symptoms. Shortly before

Microscopic drawings

of Kidney

Fig 1

Section through cortex of kidney - showing acute congestion of vessels, and cloudy swelling of epithelium of the tubules

a Glomerular tuft with capillaries engorged with blood

b Swelling of endothelioid cells of Bowman's capsule

c Epithelium of convoluted tubules shows cloudy swelling

d Intertubular capillaries engorged with blood

×500 diam

Fig 2

Section through boundary layer - showing great engorgment of vessels with blood, and cloudy condition of the tubules

a Vessels distended with red blood corpuscles and a few leucocytes

b. Ascending limb of looped tubule of Henle shows cloudy swelling

c Descending limb of tubule of Henle.

×500 diam

Fig 1.

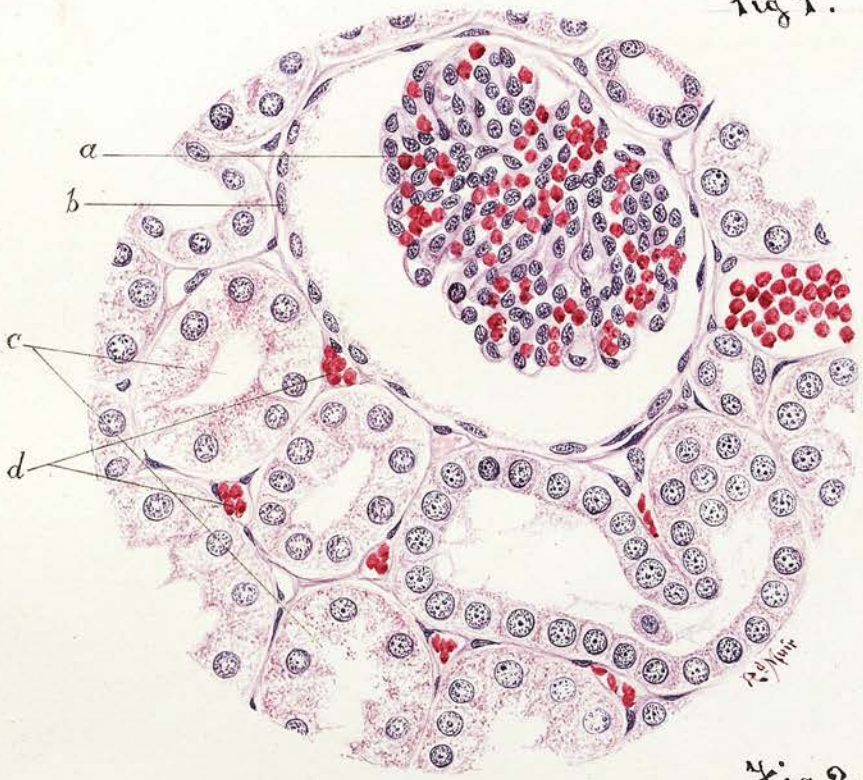
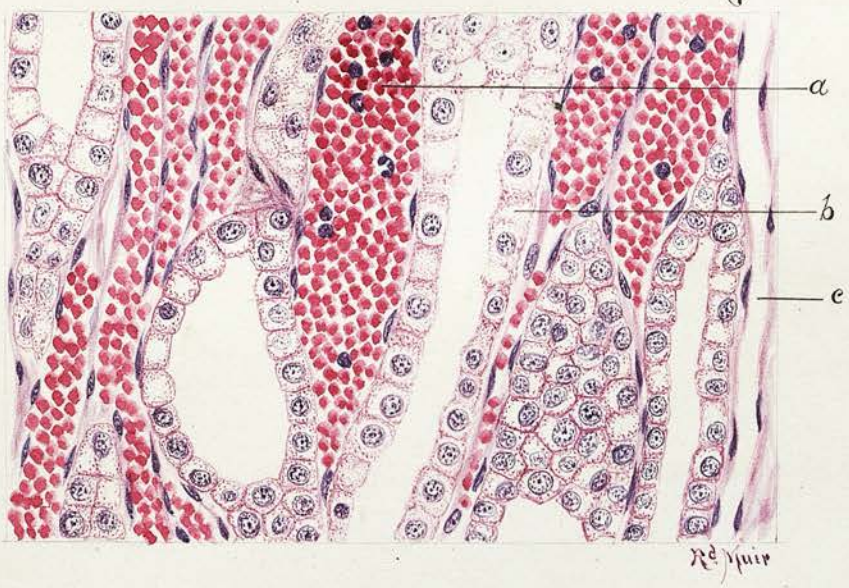


Fig 2.



death the temperature fell to about 97°F., probably due to the cold packs which had been applied to the head. I took the specimen of urine across to the University Materia Medica Laboratory and Dr. Sillar was kind enough to test the same. It gave a strong reaction of Carbolic Acid with Bromine water and Ferric Perchloride after distillation.

The Sectio showed a large thymus gland, quite normal. The liver showed well marked furrows and grooves, not unlike a syphilitic liver, but was quite normal on section. The spleen was normal. The kidneys looked quite normal and showed absolutely no catarrhal or other evidence of inflammation on naked eye examination. Microscopically:- Sections of the right kidney (see diagrams and Slides) show well marked cloudy swelling and destruction of the epithelial cells of the tubules, all the nuclei of which do not take on the stain; there is marked congestion of the blood vessels, in some places amounting to slight haemorrhage, especially into the lumen of the tubules. The capillary tufts are very much retracted from Bowman's capsule, which is considerably thickened, owing to the proliferation of the cells lining it.

In other words, the appearances are all those of an acutely inflamed kidney.

Remarks:- Since disinfection of the skin in the immediate neighbourhood of the site of an operation is of the utmost importance before commencing to wound the integument, it has been customary in these wards to apply to it after having been washed, a poultice of Carbolic Acid of the strength of about 1 in 40 or weaker, but never stronger, for a variable time on the night previous to the day of operation, and to renew the same again immediately prior to the operation. It will be noticed that a very weak Carbolic Acid lotion (1 in 60 or 70) was employed in my case, whereas in those of Lucas and Lane a 5% solution had been made use of; and in the cases of the two journeyman joiners to be mentioned later on, even a still stronger solution (1 in 8) of Carbolic Acid was employed. It was difficult at first to understand why this child should have absorbed such a large quantity of Phenol as to prove fatal, since many hundreds of patients, young and old, have been similarly prepared, and beyond the case I have just related I know of no other cases, at least not in these wards, that have presented such serious symptoms. But judging from the delicacy of the infant's skin and from the amount of surface that was covered, it will be readily

seen from the results of my experiments, which will be detailed later on, that such an intoxication was quite possible apart from any idiosyncrasy, and I have no hesitation in stating that the child died from the toxic effects produced by the absorption of Carbolic Acid applied externally.

Anything more distressing could scarcely be conceived than for a case such as this to occur in private practice. Happily, this peculiar susceptibility to poisoning by Phenol must certainly be of rare occurrence, or it would have been noticed earlier among the large number of patients that have been treated likewise.

LITERATURE.

When first introduced as a curative agent, Carbolic Acid was considered harmless by the great majority of surgeons, but shortly after its introduction into the practice of Surgery by Lister, it was noticed that valuable as are its effects in some directions, so it can be injurious to the human organism in others. Even as far back as its discovery in 1834 by Runge of Oranienburg (Ann. d. Phys. und Chem, Bd. 31., 1834. S.65; & Bd.32., S.304.) to whom its antiseptic properties were known, its poisonous effects, when externally applied, were noticed by Binz. In his"Lectures on Pharmacology", when discussing Phenol he describes the death of a dog which had been washed with a watery solution of it to destroy the fleas on his body. About 1 hour after the bath, the animal was found lying on its side and foaming at the mouth and in this state it died. Since then numerous other similar toxic effects in animals have been recorded by Lightfoot (B.M.J. II, 1870 p.331.) Its application as a vermicide was not confined to animals alone, but very soon found use in human subjects suffering e.g. from Scabies. Thus, in 1868 shortly after Lister's great advance in antiseptic

Surgery, 3 such cases of Carbolic intoxication, 2 of whom proved fatal, (B.M.J. I., 1868, p.220.) are mentioned as having resulted from the rubbing in of Calvert's impure Carbolic Acid by an error of the nurse. And a few years later Kohler (Wurtemburg Med. Correspondblatt. XLII, 1872, S.41-49: Hoppe-Seyler Archiv. f.d. ges Physiolog., Bd.V., 1872, S.470; Schmidt's Jahrbuch, Bd.CLV. S.276) reported his two well known cases of Carbolic poisoning, by the skin absorption of a watery solution, in 2 journeyman joiners suffering from Scabies, but otherwise healthy. They rubbed themselves almost completely over the whole body with a solution of 30 grams of Carbolic Acid to 240 of water, or a strength of 1 in 8. One of them died while the other recovered. Besides these cases just related, numerous other intoxications in human subjects from the absorption of Carbolic Acid in its external application for Scabies have been reported. And when Lister's antiseptic treatment of wounds became more widely employed in the practice of Surgery, cases of poisoning, some of them fatal, in which the patient, either at the time of operation or subsequent to it, had Listerian treatment thoroughly carried out, became more common and sometimes caused

the surgeon a great deal of anxiety. Its value in the treatment of wounds and in the purification of the site of operation was none the less. Lightfoot (B.M.J. II, 1870, p.331) notices a case (not fatal) of poisoning, from the application of a Carbolic compress of the strength of 1 in 50 of water, to an elbow operated upon, and Wallace (B.M.J. I, 1870, p.432) mentions a similar instance from a Carbolic dressing of 1 in 8 of olive oil in Hip Joint Disease. It will be unnecessary to detail any more such cases but it will be sufficient to place on record the following references:-

Wood: Principles & Practice of Therapeutics, 1888, p.604. Fatal poisoning in a child sitting upon a block upon which some of the acid had been thrown.

B.M.J., March, I, 1873, p.226, Death from absorption by a wound 4 inches long.

New York Medical Gazette, April 1871.

Guy's Hospital Reports, 1877.

Simon: London Medical Record, Oct.15, 1887, p.465. Infant poisoned by the use of carbolised cotton wool.

New York Medical Journal, Nov.30, 1890, Child 7 months old.

Langenbuch: Berliner Klin: Wochenschr: Bd.28. 1878, S.412.

Falkson: Archiv. f. Klin. Chir. Bd.26, 1880, S.204

Langenbuch subsequently in his operations, as a prophylaxis protected the surrounding skin by means of gutta-percha closely applied, and since then has not met again with any evils. He quotes (L.C.) the death of a young girl, 5 years of age, in whom a linear incision was made to let out the pus from an abscess about the hip, and apart from previously disinfecting the skin and the application, subsequent to the operation, of a 5% (L.C., S.414) carbolic gauze wrung out of a 2% carbolic lotion and extending to about the middle of the thigh, Carbolic Acid was not allowed to come further into contact with the area. Falkson (L.C.) in his researches on the quantitative estimation of phenol in the urine after operations or during the treatment of wounds by Lister's method, showed that even so much as 5.3871 grammes Phenol could be excreted within the 24 hours and yet not seriously affect the patient. He also mentions 4 cases, as having died purely from Carbolic intoxication that resulted from the operation.

And within recent years evils not only resulting in intoxication, but even in actual death, have followed the preparation of the skin for operation in the usual way. We notice the 3 cases of Lucas and

Lane, ~~and have~~ already referred to in the introduction, resulting from disinfection of the skin by means of Carbolic compresses of the strength of 1 in 20. And although in the whole of the literature upon the subject I have only been able to find a single reported fatal case that resulted from a watery solution applied to an entirely unabraded skin (I refer to one of the journeyman joiners of Köhler), yet there were numerous that resulted from the application of a solution of carbolic oils of various strengths. In all the other fatal ones that resulted from watery solutions there had always been some wound or abrasion of the skin. Even the death of an infant a few days old, quoted by Cohn (Vierteljahrschr. f. Gerichtl. Med., Berlin, 3F. XI 1896, S. 307-309.) as having resulted from the external application of phenol, was complicated by a raw navel.

From the cases quoted it will be noticed that nearly all the fatal and the majority of other cases of poisoning that recovered, have occurred in infants, young children and adolescent females. And in a very interesting article in the Berlin Klin. Wochenschr. Bd. 28, 1878, S. 413, Langenbuch pointed out the greater susceptibility of infants, young children, females and debilitated adults as compared with healthy adult

males, thus supporting the popular view held, with regard to the absorption of Carbolic Acid from the skin, viz. that the more delicate the skin is and the weaker the constitution, the greater are the chances of intoxication.

It was first definitely recognised in 1851 that Carbolic Acid is a normal constituent of animal urine. It was Stadeler (Ann. d. Chem. und Pharm. Bd., 77. 1851. S.17) who then demonstrated its presence in the urine of an ox. While shortly afterwards its occurrence in normal human urine was recognised by Baumann, Salkowski, Hoppe-Seyler, Brieger and others, and its increase in disease by Salkowski (Ber. d. d. Chem. Ges. IX. S.1595), Brieger & Hoppe-Seyler (Zeitschr. f. Phys. Chem., Bd. II. 1878, S.242). As such it appears only in very small quantities, the average daily excretion in a healthy subject on a mixed diet being, 0.05 to 0.07 grms. (Strasser, Zeitschr. f. Klin. Med., Bd. 24, 1894, S.547; Brieger, Zeitsch. f. Phys. Chem. Bd. 2, S.241; Munk, Pfluger's Arch., Bd. 12, 1876, S.145.), and in herbivora the quantity excreted is greater than that of carnivora. (Brieger Zeitsch. f. Phys. Chem. Bd. 2, 1878, S.234; also Zeitsch. f. Klin Med., Bd. 3, 1881, S.468

As is well known, the Phenols, (Phenol, Para-kresol, Hydrochinon & Pyrocatechin) that become excreted in the urine occur as Ether-Sulphuric Acid salts (Baumann, Pfluger's Arch. Bd.12, 1876, S.69) and not as pure Phenol (Buligwisky, Med. Chem. Untersuchungen Hoppe Seyler, Bd.2, 1887, S.243.) Free Carbolic Acid never occurrs in the urine but is found in the faeces, which then, as well as the expiratory air and sweat of the person, can show a strong smell of Carbolic Acid. Where, however, this combination with Sulphuric Acid takes place is not definitely known. Perhaps the kidneys (Strasser, Zeitsch. fur Klin. Med., Bd. 24, 1894, S.547.) may account for some of the Phenol compounds found in the urine; but it is also possible that the liver (Baumann, Pfluger's Arch. Bd. 13, S.287.) may be the seat of this change. Neither is it certain that all the Phenol is transformed into Phenol-Sulphuric acid, since when there is not a sufficient quantity of sulphates, the Phenol combines with Glycuronic Acid and becomes then excreted in the urine as Phenyl-Glycuronic Acid. (Kulz, Zeitschr. f. Biol. N.F. Bd.9 1890, S.249; Brieger Zeitschr. f. Phys. Chem. Bd.2 1879, S.243; and Zeitschr. f. Klin. Med., Bd.3, 1881 S.468). The quantity of Phenol excreted is not to

be taken as the total quantity of Phenol passing through the organism, since a portion of it becomes oxydised into Oxalic Acid (Salkowski, Pfluger's Arch. Bd. 5, 1872, S.357) and Benzoic Acid and excreted as Hippuric Acid (Strasser, Zeitschr. f. Klin. Med., Bd. 24, 1894, S.544.) and into other completely oxidised bodies; while a portion too becomes oxidised into Hydrochinon and Pyrocatechin, these ultimately appearing in the urine as Phenol-Sulphuric Acid compounds (Baumann & Preusse, zu Kenntniss der Oxydationen und Synthesen im Tierkorper Zeitschr. f. Phys. Chem. Bd. 3, 1879, S.156.). It is to these oxydation products that the characteristic brown or green colouration of the so-called "Carbolic urine" is due. Besides being excreted in the urine part also becomes eliminated by the faeces, sweat glands, saliva and breath. The question therefore arises for solution as to how much of a known quantity of Phenol becomes excreted by the kidneys. In their experiments on animals Schaffer (Journal f. Prakt. Chem., Bd. 18, S.282) and Salkowski (Centralblatt. f. d. Med. Wissenschaften Bd. 31, 1878) showed that, of the quantity of Phenol administered never more than 70% of it reappeared in the urine; and these authors also concluded that,

owing to the Ether Sulphuric Acids being considerably more increased than the original quantity of Phenol employed would have led us to expect, some other aromatic bodies, which also become excreted as combined Sulphuric Acid, must have been formed. The fact that Phenol can be absorbed in large quantities by the unabraded skin surface was pointed out by Huseman, Hoppe-Seyler & Kohler (Huseman und Ummethan Deutsche Klinik 1870, Nr.38). These authors applying it externally to animals produced a Carbolic Acid intoxication, and further showed that, when it has thus been applied, Phenol compounds immediately make their appearance in the urine, as well as in the other above mentioned excretions, and that the greater the amount applied, the greater is the quantity excreted.

We may now consider how it becomes absorbed. This cannot take place as unchanged Carbolic Acid , Firstly, because it seems highly improbable that it passes into the circulation uncombined, for in that state it would coagulate the albumen of the blood; secondly, because its presence as such in the blood has not yet been demonstrated; and lastly, because it does not appear as such in the urine, but as a Potassium Ether-Sulphuric acid salt. In some form

or other, therefore, it must be absorbed. A remarkable fact in Phenol absorption is, that, while it is undoubtedly excreted by the kidneys and other channels, yet sometimes no traces of it have been found in the blood. Baumann (Pfluger's Arch. Bd. 13, 1876, S.285.) demonstrated the presence of Ether-Sulphuric Acid in the blood of animals, which have had Phenol administered to them in their food, while later on the same author in conjunction with Christiani (Zeitschr. f. Phys. Chem. Bd. 2., 1878, S.350, cf. Hoppe-Seyler, Pfluger's Archiv. Bd. V. S.176.) failed to detect Ether-Sulphuric Acid in the blood of a newt, notwithstanding its occurrence in the urine of the animal. Likewise Labbe & Hoppe-Seyler (Pfluger's Arch. Bd. 5, S.426.) affirm that the blood of the higher animals poisoned by Carbolic Acid presents nothing abnormal and that the substance is eliminated probably as an alkaline carbolate.

Its absorption by the skin is probably affected by the sudorific and sebaceous glands (Langenbuch, Berlin, Klin. Wochenschr., Bd. 28, 1878. S.412) and this absorptive power led Lister to use it to purify the skin and as a method of treating subcutaneous inflammations. Langenbuch holds that by opening

the pores of the skin, as by stretching or shaving and scrubbing it, an increased absorption takes place, sometimes amounting to a Carbolic Acid intoxication. The former he illustrated by the case of a woman, 28 years of age, in whom a large extent of skin surface had been removed in an operation and been substituted by a transplanted flap. This latter became somewhat tightly stretched when stitched in position and had a 2½% lotion of Carbolic Acid applied to it. On the night of the operation she developed symptoms of Carbolic Acid poisoning, which, however again subsided when the flap was loosened and allowed to retract. He further pointed out that the absorption from the unabraded skin is considerably greater than that from a wound, and thus by protecting during operation the surrounding healthy skin by guttapercha tissue, he diminished his risk of intoxication which he otherwise found difficult to avoid when thoroughly carrying out the Listerian method.

When Phenol is absorbed in considerable quantity the salts of Sulphuric Acid disappear from the urine, until, when the poisonous symptoms are at their height, not a trace of them is present. (Baumann, und Herter, Zeitschr. f. Phys. Chem. Bd. 1. 1877; Baumann, Pfluger's Archiv. Bd. 13, 1876, S. 285; Christiani, Zeitschr. f. Phys. Chem. Bd. 2, 1878. S. 273.)

A patient can therefore tolerate Carbolic Acid better when, simultaneously with the acid, Sulphates are administered (cf. Brieger, Zeitschr. f. Phys. Chem. Bd. 3, 1879, S. 148).

I have thus far dealt with the constitutional effects of the drug when externally applied. I shall now revert to its local manifestations, since these are sometimes quite as alarming to the surgeon. As this, however, bears but slightly, but yet very decidedly, on the special aspect of the subject I am dealing with, I shall dispose of it very briefly. When applied locally it may produce a necrosis (gangrene) or an acute inflammatory eczema, with the common occurrence of which, every medical man ought to be familiar. The unfortunate results from its injudicious use that often occur are far from being pleasant. The digits show a more marked predisposition to gangrene than any other part of the body, and more particularly as pointed out by Leusser (Munch. Med. Wochenschr., Bd. 43, 1896 S. 338), in infants, young children, women and feeble or debilitated male adults. This author quotes no less than 48 such cases (L. C.) and to these I may add 2 which came under my own observations in the Out-patient Department of the Edinburgh Royal Infirmary

during the winter of 1897. The first was that of a child 3 years old, who had cut her little finger; this was dressed with a Carbolic oil poultice by a druggist, and when I saw it 14 hours after the application the 2 terminal phalanges were quite benumbed and whitish, and in spite of treatment ultimately became gangrenous. The other was that of a strong, healthy, male adult, aged 36 with a bruised left middle finger to which a Carbolic poultice of the strength of 1 in 20 was applied over night by his doctor. I saw him two days afterwards, and then found the terminal and half of the middle phalanx quite dead and black. There is no doubt that a tight bandage co-operated with this. In both cases the phalanges eventually had to be surgically removed. In the majority of cases it is generally the result of employing too concentrated solutions. This may have been applied intentionally or accidentally, as often happens when lotions are not shaken up in the bottles before use and thus allow a concentrated solution to collect at the bottom. Of this latter occurring I remember an instance of a medical man who had pricked his finger with a septic instrument and applied, as he thought, a Carbolic poultice of the strength of 1 in 20 in water, but in reality a concentrated sol-

ution, and found himself subsequently with a gangrenous finger. Not only in strong or concentrated solutions, but even when applied in very dilute solutions may it sometimes be followed by consequences as unpleasant. Thus, Frankenburger (Inaugural Dissertation, 8th Dec., 1890; Buffalo Medical & Surgical Journal, Oct. 1892.) in his experiments showed that by repeated compresses in weaker or stronger solutions, a direct damage to the red and white blood corpuscles is caused, producing a stasis, a blocking and thrombotic condition of the blood vessels, and ultimately the death of the part; and the longer the duration of the application, the deeper is the destruction. This is confirmed by Leusser, who states that the application for several hours of even a 2% Carbolic Acid solution is able to cause gangrene of a complete digital phalanx, without amounting to a caustic action as in concentrated lotions (Munch. Med. Wochenschr. 43, 1896. S.339.) The occurrence of blisters on the backs and the buttocks of patients, who had been lying during operation on cloths wrung out of a 5% Carbolic Acid lotion is not at all infrequent.

Surgeons and their assistants also experienced similar misadventures, more especially in the days

of the Carbolic spray when, there was little doubt, that many a surgeon was carried off by the lesions that resulted from chronic poisoning by it, i.e. the Carbolic Marasmus of Czerny. Till now this has been noticed only in doctors, but with the present knowledge of the dangers which the working with Carbolic Acid brings about, these cases have become very rare. Nevertheless, at the present day, surgeons and their assistants often still complain in the evening after their operation of a feeling of tiredness and sometimes a superficial pain across the sole and instep of the foot, not to speak of the anaesthetic feeling, numbness and burning pains in the hands so commonly noticed, or even the Carboluria so often produced in them (Billroth, Klin. Chir.)

We have thus noticed Carbolic Acid applied to the skin of animals or human subjects in a variety of forms, giving rise to intoxication; and there is no doubt whatsoever that one should be very careful and cautious in applying Carbolic Acid to the skin, and more especially in children.

MODE OF EXPERIMENT.

Before proceeding to explain the method adopted in making the observations on the subjects as well as the precautions taken to ensure uniformity and prevent any exception being taken to my mode of procedure, I shall give a short description of each of my subjects of experimentation, thus"-

1. A.Ego. Medical Practitioner, aet. 26; healthy, but somewhat thin, appetite good, bowels regular, skin resembles that of an ordinary male adult, urine normal.

2. B. Medical Student not at present engaged in handling Carbolic Acid or working in Surgical Wards. Male, aet.22, healthy and well developed, appetite good, bowels regular, skin somewhat soft, with a considerable amount of subcutaneous adipose tissue, urine normal.

3. C. Medical Student, M. aet. 37, not at present engaged in handling Carbolic Acid, or working in Surgical Wards, healthy and well developed, skin like that of an ordinary male adult skin, appetite good and bowels regular, urine normal, but shows a slight trace of phosphates.

4. D. Child, male, aet. 11 years, confined to bed with a fracture of the leg. Well developed, well-nourished and other-wise quite healthy, appetite good, and bowels regular, soft fine skin, urine normal.

5. E. Child, male, aet. 6 years, confined to bed after an operation for double Talipes-Equino-Varus. He has a small sinus in either foot which is being dressed with Mercuric Chloride solution and Corosive Sublimate wool. Otherwise, he is quite healthy and strong; but not so well developed as D., soft, fine skin, appetite good, bowels regular, urine normal.

6. D.K. Child, male, aet. $8\frac{3}{4}$ years, confined to bed with Postural Scoliosis. Fairly well developed and well nourished, muscular. Very soft, fine and delicate skin, appetite good and bowels regular, urine normal.

7. G. Surgeon, strong, healthy, and muscular, bowels regular, urine with some phosphates.

8. H. Surgeon, strong healthy and muscular, bowels regular, urates present in the urine.

From these descriptions it will be noticed that for my experiments, I selected perfectly healthy subjects, so as not to complicate matters with effects which disease might produce, since it is known that the quantity of Phenol found in the urine is affected

by various morbid conditions, as pointed out by Strasser (Zeitschr. f. Klin. Med. Bd 24, 1894, s. 543.). This author has definitely demonstrated the increased or diminished excretion in the urine of Phenols in certain diseases, and thus we can well understand that these undoubtedly might more or less affect the quantity of Carbolic Acid absorbed from the skin and excreted in the urine. For this same reason the applications were made to healthy unabraded skin, since it has been held that poisoning by absorption from external applications is almost entirely from the skin; and by means of protecting the surrounding skin with ~~the~~ guttapercha, it can be demonstrated that only slight absorption of Carbolic Acid takes place through the wound and that it mostly is effected by the surrounding skin. (Laugenbuch Berlin, Klin. Wochenschr. Bd 28, 1878, s. 412).

That the difference in the absorbing power between a soft, fine, delicate skin, and one of coarser texture, such as that of an ordinary adult male, might be manifested, children were chosen to represent the former class, and male adults on the other hand, the latter.

As regards delicacy and softness , the skin of the child would also fairly well represent that of females and so serve as an indication of the absorption from such skin surfaces.

The method followed in my experiments has been arranged to assimilate the conditions, under which they are made, as far as possible to the conditions found in the practice in the wards of an hospital on the one hand and in private practice on the other; not that there is any material difference between the two, but simply because many a time in private practice and more especially with women patients, one has not an opportunity of so thoroughly purifying the skin as in an hospital. And the precautions taken to ensure that the results of my experiments might represent as nearly as possible, what actually takes place, when, prior to an operation, Phenol is applied as a disinfectant and antiseptic to the skin surface, are given in the following detail:-

All through my experiemnts, as the site of my applications, I selected the front aspect of the thigh, and always in each individual case used the leg that was employed for the first experiment on that subject.

In order to ascertain the difference in the amount of absorption between a pure and an impure Phenol, both varieties were tried. The pure Phenol was that of Barron Harvey & Co., with a melting point of 40.9°C for 5 readings, taking the melting point as the best standard for purity. It showed no pink colour on exposure to air, and was also free from impurities in other respects. As an impure Phenol I employed Calverts No. 4 Carbolic Acid. The solutions were made up by weighing a quantity of Phenol, which had been dried over-night over Sulphuric Acid, and then dissolving it in cold, sterilised, distilled water, to avoid any volatilization by heat, until the given strength is reached.

In private practice there is not always an opportunity for having the skin thoroughly prepared, so the best means at hand must be had recourse to. Thus many surgeons give the patient a hot bath previous to applying the poultice, or it may be that the skin is simply washed with hot water and soap to remove the surface grease. In some of my experiments, viz., from 13 to 118 inclusive, I adopted this method. In other cases I followed out strictly what is customary in wards 15 and 16 of the Edin-

burgh Royal Infirmary in thoroughly disinfecting the skin. The part to be prepared is cleansed firstly by shaving it, and then scrubbing and washing it up with soap, hot water and a nail brush. Next it is washed with Ether, and thereafter a poultice of Sodium Bicarbonate is applied for 3 or 4 hours. After removal of this, the skin is again wasked with soap, hot water and nail brush, and lastly again scrubbed up with Ether. To the skin thus prepared, the poultice was applied as follows:-

A double layer of Surgeon's lint was taken according to the size required. This was soaked with the given quantity of Carbolic Acid solution. Neither too much nor too little was put on the poultice. I ascertained beforehand how much fluid the particular size of lint could absorb easily, so as not to part with any of it except when extra pressure be applied. Having measured the liquid I immediately emptied it from the C.C. measure upon the lint and by means of finger pressure uniformly distributed it through the material, allowing half a c.c. for what adhered to the fingers and sides of the measure, as that amount was found by practice to be lost in that way. The lint was at once placed

upon the skin laid out flat and covered with white jaconet, this last being larger than the lint by extending about 2 ins. beyond it on all sides. The whole application was bandaged with a 3 inch domette bandage to the limb with a uniform amount of pressure, not too great that the blood might be pressed out of the part, but with a tension just sufficient to maintain the poultice in position and in accurate contact with the skin. The Carbolic Acid poultices were applied when the patients were at rest, so that the absorption might take place under uniform conditions, and so that uniformity in the state of the circulation of the skin might be secured, because when a person walks about, more blood is brought into the limbs and hence the absorption might be more active. Again to follow out what is normally done in surgical practice the poultices were applied during the night time, and since the skin is more active in the absence of active digestion, the applications were made two or more hours after meals and before next meal. And of great importance was that no Carbolic Acid was allowed to come in contact with any of the subjects, beyond what was applied in the experiments. The children, however, could not under the circumstances present,

have been kept away from a Carbolic Acid atmosphere, such as is generally present in a surgical ward.

In the case of the adults, the urine was collected by themselves, full instructions having been given to them how to proceed. As to the children, owing to the difficulty of collecting the entire quantity of urine from them while going about, some who were confined by injuries to bed were secured and a special day and a night nurse were employed to see that their urine was collected. In each case the collection was made from the time of the application until 24 hours after its removal because it has been shown that within this period the entire quantity of Phenol becomes excreted (Salkowski, Pflüger's Arch. Bd. V. 1872, p. 355; and Kruppke ibid). In the case of children this collection was sometimes impossible to be carried out owing to inability or unwillingness on their part to micturate within the set time. A longer time was therefore allowed in such cases, but allowance was made for the normal amount of Phenols in their urine during this extra time. Lastly one or more days were always allowed to intervene between two applications.

TESTS FOR THE QUANTITATIVE ESTIMATION OF PHENOL EXCRETED IN THE URINE.

Of the various qualitative tests for Phenol of which the Ferric Perchloride, the Ammonia and Calcium Chloride, the Nitric Acid and Potassium Hydrate, the Mercury Nitrate with nitric and nitrous Acids (Millons Reagent) tests are the most important, none are of sufficient delicacy for this work; and since they do not lend themselves to aid in the quantitative analysis of Phenol, they were not employed. Several other methods, however, have been put into practice for the estimation of the quantity of Phenol found in the urine. Some of these proceed by the Gravimetric, others by the volumetric system. Whichever system is adopted, they all with one exception depend on the property Phenols have of forming insoluble compounds with Bromine and Iodine. I shall therefore take a review of the more important of these methods of analysis.

I. That method of estimating the amount of combined Sulphuric Acid. According to Baumann (Pflüger's Arch. Bd. 13 s. 276) 0.346 grms. of this is equivalent to 0.332 grms. Phenol. what?

II. Landolt's Method by the Gravimetric System (Berliner Chem. Bericht Bd. IV. 1872 s. 772). Landolt was the first to precipitate Phenols, with Bromine water. He then weighed the Tribrom-Phenol, 331 parts by weight of which correspond to 94 parts by weight of Carbolic Acid. By means of this method 1 part of Phenol in 57,000 of water can be detected, the solution being rendered turbid.

This test, however, cannot be held to be a very satisfactory one, since, if allowed to stand for some time, in addition to the Tribrom Phenol, other compounds which are rather unstable, such as the Tetra- and Pentabrom-Phenols, are apt to be formed (Bericht der Deutsch. Chem. geselsch. Bd. IV. 1872 s. 771).

III. Koppeschaar's Method (Zeitsch f. Analyt. Chem. Bd. 15, 1876 s. 233). This is also based on the formation of Tribromphenol, but differs from that of Landolt in proceeding on the volumetric principle. Koppeschaar instead of weighing the precipitated Tribromphenol adds a known quantity of Potassium Iodide solution to the Bromine solution and then titrates back with Sodium Thiosulphate solution the free Iodine that resulted from the formation of Potassium Bromide. Both the foregoing reactions take place in the cold.

IV. Messinger and Vortman's Method (Bericht. d. Chem. Gesch. Bd. 22 1889 s. 2313).

A better method than either of the foregoing is that of Messinger and Vortman who tritrate with Iodine in presence of heat (60°C), instead of Bromine in the cold; and then, from the quantity of uncombined Iodine titrated back with Sodium Thiosulphate solution, calculate the qunatity of Iodine that has gone to form Triiodide of Phenol. The precipitate is filtered off, but in so doing, a certain amount of Iodine gets lost and thus lessens the value of the test.

V. Penny and Kossler's Modification of Messinger and Vortman's Method (Zeitschr. f. Phys. Chem. Bd. 17 1893 s. 117-139.). Penny and Kossler after having thoroughly tested and examined the previous method, somewhat modified it by titrating in the presence of the precipitate, instead of first filtering the solution, and thus surpassed it in accuracy and simplicity. For Phenols it is by far the most delicate test, as well as a more accurate one than that by means of Bromine, since it was shown (Zeitschr. f. Phys. Chem. Bd. 17, 1893 s. 135) that, where Bromine water failed to give any precipitate, as in

the case of the last 3 distillates for titration, referred to in the description given later on, of an actual experiment, Iodine still precipitated an amount of Triiodide of Phenol equal to one third of what is found in the first 3 distillates. Besides in this method we are not dependent upon the amount of precipitate formed, as in the case with the Bromine test, which should be added only until there is no more cloudiness. But Iodine on the contrary may be added until eventually no more enters into combination with Phenol to form the Triiodide of Phenol. One cubic Centimetre of decinormal Iodine solution corresponds to 1.567 mgrs. of Phenol, or 1.8018 mgrs. of Parakresol. Therefore the total number of C.C. of Iodine solution entering into combination, multiplied by these figures will give the amount of Phenol or Parakresol respectively in Milligrams.

In all my experiments I followed this last method for the quantitative estimation of Phenol very closely.

AN EXPERIMENT.

Before proceeding to the actual experiments with urine containing Carbolic Acid, and in order to thoroughly acquaint myself with the method of procedure, as well as to test the accuracy of my reagents, I undertook a series of experiments with known quantities of pure Phenol and obtained results, almost identical with those given by Penny and Kossler (Zeitschr. f. Phys. Chem. Bd. 17, 1893 s.124), as will be observed from the following Table I.

TABLE I.

	Phenol employed. Mgrms.	$\frac{1}{10}$ n NaOH cc.	$\frac{1}{10}$ Iodine cc.	$\frac{1}{10}$ n Iod. consumed cc.	Phenol found mgrs.	Quantity obtained by Penny & Kossler, the same amount employed. Mgrms. Phenol.
(6)	15	5	20.00	8.95	14.02	14.10
(8)	15	5	20.175	9.00	14.10	14.10
(11)	15	10	23.40	9.025	14.14	14.88
(13)	15	15	30.175	9.50	14.88	15.27
(14)	15	20	35.50	9.50	14.88	15.19

The slight deficiency on my part, as compared with the results obtained by Penny and Kossler, must have been due either to my Phenol not having been absolutely pure, or to my measurements not being absolutely correct, for it is not likely, that the error should have arisen with such expert chemists, as these gentlemen. However, it is so trifling that it may safely be disregarded.

When the Phenols in the urine are to be quantitatively estimated, we must first liberate them from their nonvolatile Ether-Sulphuric Acids by means of some mineral Acid and then subject them to distillation, when only Phenol and Parakresol will come over in the distillate - the Dioxy Benzols, Hydrochinon and Pyrocatechin, not being volatile - and can be determined by the usual methods. But to obtain accurate results, two points must be observed, viz., firstly, that the Phenols be completely distilled over and secondly, that the Urine contain no substances, but Phenols, which will either fix Iodine or decompose the Potassium Iodide, used in titration, thereby liberating Iodine. To the former of these belong chiefly Acetone, Ammonia, Formic Acid and according to some, Acetic Acid; and to the latter Nitric Acid.

The Acetone is got rid of by simply evaporating the urine in an alkaline solution to about one-fifth of its quantity. When now 5% Sulphuric Acid be added to this concentrated Urine, it not only serves to decompose the Ether-Sulphuric Acids, but also suffices to fix all the Ammonia. Should any Formic Acid or Nitric Acid have been present in the urine, their distillation cannot be prevented otherwise than by the redistillation over an excess of Calcium Carbonate, which fixes these two Acids, but not the Phenols.

In estimating the quantity of Phenols found in the urine I adopted the method of Volumetric Analysis of Messinger and Vortman as modified by Penny and Kossler (Zeitschr. f. Phys. Chem. Bd. 17, 1893, p. 124) viz. by adding excess of Iodine in an alkaline solution of Sodium Hydrate so as to form the Triiodide of Phenol. Known quantities of these are added, and the free Iodine, that has not been consumed by the Phenol, is titrated back with a solution of Sodium Thiosulphate. Knowing therefore, the whole amount of Iodine used, and how much of it was free, one can find the quantity that must have gone to combine with the Phenol; and since this takes place in a definite

proportion, viz., 1 molecule of Phenol for every 6 atoms of Iodine, according to equation, $C_6H_5OH + 3I_2 = C_6H_2I_3OH + 3HI$. the total quantity of Phenol can be ascertained.

From this general plan of procedure a detailed account is now given, with a statement of precautions to ensure accuracy. The urine having been collected for the 24 hours after the removal of the application, 500C.C. of it are taken. This quantity, after being weakly alkalised with Potassium Hydrate, (B.P. solution) is evaporated down to about 100 c.c. This serves not only to set free the Acetone present, but also according to Munk to produce the greatest possible quantity of Phenol, for he showed that a urine previously evaporated down yields more Phenol than a non-concentrated urine (Arch. f. Anat. und Phys. Chem. Supplement 26 1880; Pflugers Arch. Bd. 12, 1876 s.145). To the 100 c.c. of concentrated urine pure Sulphuric Acid is added to the amount of five per cent of the original 500 c.c. that is to say 25 c.c. Sulphuric Acid. This decomposes the Ether-Sulphuric Acid having the formula $C_6H_5O.SO_2OH$ or $(C_6H_5)HSO_4$. which, as already stated, is the form in which the Phenol becomes excreted in the urine. Immediately the strong acid is added the liquid blackens. When

shaken up it acquires a pungent odour, considerable heat being evolved. For this last reason it is advisable previously to cool the concentrated urine, as this extra heat might be sufficient to raise the fluid to such a temperature as to drive off some of the Phenol. I then allow time for cooling, as well as for a thorough reaction (Hoppe Seyler Pfluger's Arch Bd. 5, 1872 s. 472), then shake up and distill over 100 c.c. To the residue I add another 100 c.c. of distilled water, with which the evaporating capsule has been rinsed, thereby removing any traces of Phenol Compounds adhering to it, and again distill over 100 c.c. Repeat the process altogether six times (Penny and Kossler Zeitschr. f. Phys. Chem. Bd.7, 1893, s. 135), and thus obtain six separate distillates and a final residue of a black tarry appearance, having a strong and unpleasant odour. These six distillates have each a distinct aromatic odour, and of the six the last three contain about one-third of the quantity of Phenol present in the 500 c.c. of urine . The colour of the first distillate varies from a faintly yellow to a dark amber ~~colour~~, due to urine pigment, while the remaining five are quite clear. Very nearly all the Phenol goes over in the first distillate, hence the import-

ance of collecting it carefully. At the commencement of the distillation and towards its completion the flame is to be kept very low, since, with great heat, the contents of the flask are liable suddenly to rise up and boil over. For these distillations I always employed Kjeldahl flasks and bulb-distillation tubes, fitted with rubber corks, to guard against the explosion and bobbings, which arise from the concentrated urine and the strong Sulphuric Acid, and also to prevent any Phenol escaping. The receivers were placed in the ordinary manner, since no Phenol is lost by leaving the same uncorked (Zeitschr. f. Phys. Chem. Bd. 17, 1893 s. 137). To free these distillates from the Formic and Nitric Acids, which might be present, I redistill them over an excess of Calcium Carbonate as follows:- The first three distillates are placed in a Kjeldahl flask and pure precipitated Calcium Carbonate is added until the acid reaction has disappeared. This can be recognised by the Carbonic Anhydride ceasing to come off, and also by the presence of an excess of Calcium Carbonate, imparting to the fluid either an opaque white or opaque orange colour, the particular shade of colour depending on that of the first distillate.

I now distill over till the residue is just free from dryness. In this process there is not the same risk of spirting over, which existed at the first distillation. The liquid, which I have thus obtained and which I named Distillate A, forms the first Distillate for Titration.

To the residue in the flask, the three remaining distillates are added, with some more Calcium Carbonate, if necessary. Distilling over as before, I obtained my second distillate for titration or Distillate B.

I now proceed to the titration of these two distillates named A and B. The first Distillate for titration (A) is divided into 4 equal parts. Two of these parts are reserved, in case any mishap should befall the other two, which are treated with different quantities of the testing solution, so that when the end results correspond, one knows definitely that a sufficiency of reagents has been added in either case: thus (c.f. experiment 44B, if 15 c.c. of decinormal Sodium Hydrate Solution and 30 c.c. of decinormal Iodine Solution be added to the one part; and 20 c.c. of decinormal Sodium Hydrate Solution and 40 c.c. of decinormal Iodine Solution to the other,

and an equal result be obtained, I can be absolutely sure that the 15 c.c. of decinormal Sodium Hydrate and 30 c.c. of decinormal Iodine Solutions were quite enough to take up all the Phenol present; and thus I know that the total quantity of Phenol has entered into combination. Commencing therefore with my first Distillate for titration (A), I add decinormal Sodium Hydrate Solution to two of the four equal portions referred to above, and placed in bottles with accurately fitting ground glass stoppers, to prevent the escape of any Iodine vapour during the heating process. The liquid is then heated to about 60° C in a water bath for sometime, since reaction takes place more strongly and more quickly under these circumstances (Zeitschr. f. Phys. Chem. Bd. 17, 1893 s. 127). To the fluid, while still hot, I now add decinormal Iodone Solution, quickly reinsert the stoppers and replace the bottles in the water bath for about 15 minutes. In the first place, the Sodium Hydrate and the Iodine react; Sodium Iodide and Sodium Hypoiodite (Zeitschr. f. Phys..Chem. Bd. 17 1893 s. 121) are produced according to the following equation:- $2\,NaOH + I_2 = NaI + NaOI + H_2O$

The Hypoiodite thus formed combines with the Phenol,

forming Triiodide of Phenol according to

$$C_6H_5OH + 3NaOI = C_6H_2I_3OH + 3NaOH.$$

After being removed from the water bath the bottles are allowed to cool and then thoroughly shaken up to wash off the Iodine adhering to the sides of the bottles. The contents are acidulated with dilute Sulphuric Acid to decompose the Sodium Iodide and the uncombined Sodium Hypoiodite and thus liberate all the Iodine that has not combined with the Phenol.

$$NaI + NaOI + H_2SO_4 = I_2 + Na_2SO_4 + H_2O$$

The Triiodide of Phenol is soluble in Sodium Hypoiodite Solution; and the Phenol enters into combination more freely when there is also a considerable excess of free Iodine. So the best results are obtained when, for every molecule of Phenol, there be more than 3 molecules of Sodium Hypoiodite and the presence of free Iodine (5c.c. of decinormal Iodine Solution) (Penny and Kossler L.C. s.126). I have throughout all my experiments acted upon this and observed this proportion as accurately as possible.

If the Sodium Hydrate solution, added, has been so small in quantity that a sufficiency of Hypoiodite was not formed, then the Triiodide of Phenol becomes precipitated, forming a curdy orange or yellow

coloured precipitate floating in the liquid, according to the quantity of free Iodine present. It is unlikely that the deficiency of Sodium Hypoiodite will be owing to deficiency of Iodine solution, since a great excess of this is employed. When the orange precipitate has formed, more Sodium Hydrate can be added after the solution has been cooled until the precipitate is dissolved, and then more Iodine solution is added in proportion.

When on the other hand a sufficiency of Sodium Hydrate and Iodine solutions has been used the liquid becomes ultimately of a muddy chocolate-brown colour. By taking a known quantity of Phenol in Solution and first treating it with a small insufficient quantity of Sodium Hydrate and Iodine, so as to form this orange colouration, and then, after cooling, by adding more decinormal Sodium Hydrate and Iodine solution until, in the presence of heat, the usual brown chocolate colour showed itself, I ascertained that no error would be committed if I added the Sodium Hydrate and Iodine solutions in 2 or more stages, since for 30 mgrs. Phenol employed, I obtained 29.81 mgrs. Phenol or very nearly the same quantity as with a sufficienty in one stage. (c. f. Table II.).

TABLE II.

Number of Times Reagents were added.

Phenol Employed. Mgrs.	1		2		3		4		Phenol found. Mgrs.
	$\frac{n}{10}$ NaOH c.c.	$\frac{n}{10}$ Iodine c.c.	$\frac{n}{10}$ NaOH	$\frac{n}{10}$ Iodine	$\frac{n}{10}$ NaOH	$\frac{n}{10}$ Iodine	$\frac{n}{10}$ NaOH	$\frac{n}{10}$ Iodine	
30	5	10	5	10.125	5	10.150	5	9.6	29.81
	Orange		Orange White	c ppt.	Chocolate brown.		Chocolate brown.		
30	20	39.9	-	-	-	-	-	-	29.85

We have now present in the liquid, Triiodide of Phenol and free Iodine, as well as the Iodine liberated from the Sodium Iodide and uncombined Hypoiodide by the Sulphuric Acid. Therefore, knowing the whole amount of Iodine added, if it can be ascertained how much remains free, I shall know how much has combined with the Phenol; and since 1.567 mgrs. Phenol or 1.8018 mgrs. Parakresol correspond to 1c.c. of decinormal Iodine solution, the total quantity of Phenol can easily be calculated.

I therefore next proceed to titrate back the free Iodine by means of decinormal Sodium Thiosulphate solution (4grms. to 1000 c.c. distilled water at

15.5°C). The red amorphus Triiodide of Phenol with the free Iodine in the solution forms, as has already been stated, a chocolate brown colour. Now when the brown of the Iodine has been removed by the Sodium Thiosulphate, I shall find the chocolate brown passing into red. These colours are, however,, too much akin for the moment of the one passing into the other to be noted with accuracy. Therefore just before the whole Iodine has been taken up by the Sodium Thiosulphate, freshly prepared starch paste is added, and the blue Iodide of Starch blending with the red Triiodide of Phenol, forms a violet colour. Thus the end reaction is a sharply defined conversion from violet to red.

Owing to the small quantity of Phenol present in the second Distillate for titration (B) the latter was dealt with as a whole in a similar manner to Distillate A. Then, from the amount of Phenol found in the part of the urine examined the total quantity of Phenol is calculated.

Since Sodium Thiosulphate is hardly ever quite pure, and since I had to deal with comparatively small quantities of Phenol, I standardised the Iodine and Sodium Thiosulphate solutions, in order that I might be quite certain of the volumetric value of

these reagents. The decinormal Sodium Thiosulphate solution was standardised by means of pure ammonium Iodate, which is a much more stable compound; and in doing this care was taken to add a very small quantity of dilute Sulphuric Acid with the Potassium Iodide, in order to prevent the precipitation of the Sulphur from the Sodium Thiosulphate. Having standardised the Sodium Thiosulphate, I again standardised the Iodine against it. And to have these two solutions accurate they were made up every fortnight.

Now, with a view to ascertaining certain particulars with regard to the absorption of Carbolic Acid when applied externally, and its subsequent excretion in the urine, I have conducted a series of experiments. These were arranged in such a way as to throw light upon the following problems:-

I. By employing a solution of pure Phenol, with a melting point of 40.9°F. over healthy unbroken skin, which was washed with soap and hot water to remove the surface grease, I wish to enquire,

1. What amount of Phenol becomes excreted in the urine when I apply, to a certain area of the skin thus cleansed, a poultice of carbolic acid solution of a certain strength?

2. What difference, in the amount of Phenol absorbed and excreted in the urine, arises from applying the same quantity of the same strength of Carbolic Acid solution over the same extent of skin surface, for a length of time, twice and three times as long?

3. How a difference in the extent of skin surface covered by the poultice would affect the quantity of Phenol absorbed and excreted by the kidneys. To solve this question, I applied a certain quantity

of Carbolic Acid solution, of the same strength for the same length of time, over twice and three times the extent of skin surface, the quantity of the solution employed being proportional to the increase of the surface.

4. What alteration there is in the amount of Phenol absorbed, when the skin surface covered is diminished and the strength of the solution is increased. In other words is the same amount absorbed, when at one time a certain strength of solution is applied for a certain time over a certain area, as when, twice the strength of solution is applied over half the surface for the same period time.

5. Whether there is any difference, between the absorptive power of the coarser skin of the male adult as compared with the more delicate one of the child, when the length of time, the skin surface covered and the strength of the carbolic solution remain the same in each case.

11. Whether there is any difference between the amount of Phenol absorbed, when the skin is merely washed with soap and hot water, and when it is thoroughly "prepared" as for an operation, by being shaved, scrubbed with soap and hot water,

, washed with ether, and then by having a poultice of Bicarbonate of Soda applied for several hours, and again washed with ether when this is removed.

III. What difference, as to skin absorption, there is when pure (melting point 40.9°F.) and impure (Calvert's No. 4) Phenols are used.

IV. And lastly experiments were arranged to ascertain the amount absorbed by Surgeons during operations.

In carrying out these experiments I employed two solutions of different strengths, viz., 1 in 40 (2½%) and 1 in 80 (1¼%). There were applied in quantities of 25 c.c., 50 c.c., and 75 c.c. respectively over areas of 36 sq. ins., 72 sq. ins., and 108 sq. ins., and each allowed to remain in contact with the skin for periods of 2, 4, and 6 hours. I selected these strengths and times for the reason that these are most commonly employed in surgical practice.

Although figures are very instructive and conclusive in a scientific investigation, they are apt to be rather confusing, especially when data are very numerous and their various relations rather complicated. Therefore, to overcome this difficulty

and to lay this work in as clear a light as possible, I have, all through the discussion, arranged small tables and diagrams, by careful reference to which no one will have much difficulty in following me. I regret that my experiments with children were not so numerous, as those with adults, and as I should have wished them to be. This was owing to the fact that two of them fell ill with scarlatina. It is possible therefore that my averages in the case of children may not be quite so reliable as those with adults.

It is proper that I should mention that while the average daily normal excretion of Phenol is very fairly represented by .05 to .07 mgrs., I have, nevertheless, owing to the quantity varying so much in individual subjects, estimated the normal amount excreted in each of my subjects, so that my results might be all the more exact. The average quantity excreted by each individual will be found in Table .?

Since it is impossible in the urine analysis to estimate the quantities of Phenol and Parakresol spearately, it is always better to calculate the whole amount as Parakresol, because more then 85% of the volatile Phenols in the urine consist of Parakresol (Baumann Zeitsch fur Phys. Chem. Bd. 6,

1882, s. 183; and Brieger Zeitsch fur Phys. Chem. Bd. 4, 1880, s. 207). In my experiments, however, as will be noticed from the tables, I calculated them as Phenol, so as to have a better comparison with the known quantity of Phenol which I employed in each experiment. From the total number of milligrams of Phenol excreted in the urine, as the result of my application, (i.e. the total quantity excreted less the normal excretion for that period), I calculated the percentage excretion in the urine of what was applied to the skin; and in order to avoid repetition, I have called this "per cent" or "percentage absorption or excretion."

Further, from the total quantity, called "Total Phenol excreted" or "Total absorption," I likewise calculated the number of milligramms of Phenol which became excreted in the urine for every square inch of skin surface covered by the carbolic acid poultice. This I termed "square inch absorption or excretion," meaning of course only the quantity of Phenol that appeared in the urine, since I did not deal with the Phenols excreted by other channels.

The results of the experiments are arranged in tabular form,

Table 31 Normal Urines
Table 28 Experiments 13-118.

inclusive were made upon the unshaven skin with pure Phenol; 119-127 inclusive were carried out with pure Phenol on the shaven and "prepared" skin; in 128-131 inclusive, impure Phenol (Calvert's No. 4) was applied to the shaven skin. From this table all the other smaller ones were deduced.

To make the present enquiry as complete as possible, I shall pursue it in a four-fold manner. I shall first consider the case of a single individual, in whom there is a fair uniformity of conditions, apart from the variations to which he was subjected in the experiments, and shall study the amount of absorption or excretion in his case under varying conditions, as to, the length of time of the application of the poultice, the extent of skin surface covered by the poultice and the strength of the Carbolic Acid solutions in the Poultice. After having considered this typical case, I shall review the averages obtained from three adults, and after that, those given by three children. While the results obtained from one individual are valuable in giving some indication of the laws regulating the absorption of Phenol from the skin, we cannot rely on them as much as we can on the averages of

of a number of cases, since personal conditions and idiosyncrasies come into play so much. Then in the fourth place I shall consider the differences occasioned by variations in the nature of the skin; and to this end, I take the more delicate of the child and compare it with the adult.

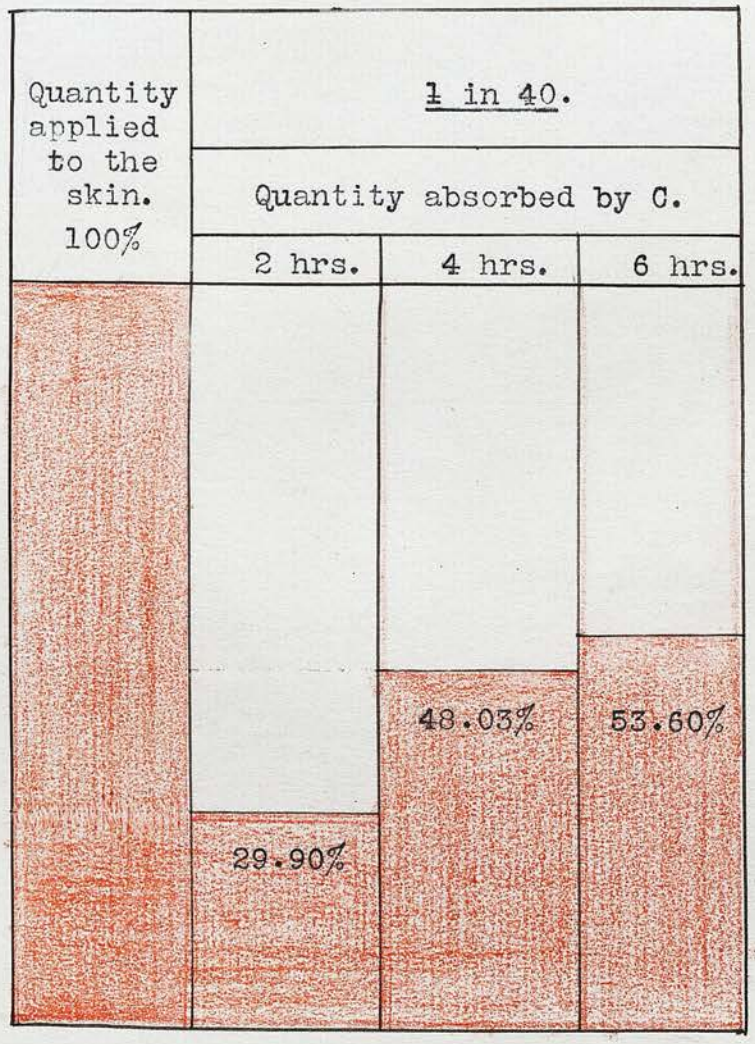
I. RESULTS OF EXPERIMENTS WITH ONE INDIVIDUAL.

I select C - the subject of experiment - as a typical case. With him the results show more uniformity than with any of the others, personal conditions and peculiarities having apparently had less influence in his case, and with him, I shall endeavour to ascertain:-

Firstly, in what manner the length of time of the application to the skin of the Phenol influences the amount absorbed; secondly, how the extent of skin surface covered alters the absorption; and lastly, what influence belongs to the strength of the solution.

I commence by considering the effect of time, and take, first, a solution of the strength of 1 in 40. Now, by applying a compress of 1 in 40 solution over any surface for 2 hours, I get an average absorption of 28.9%, or 5.02 mgrms., per sq. in. (c.f. Table I.) (That is, the percentage of the original quantity of Phenol applied in the poultice, which becomes excreted in the urine; and Milligramms of Phenol which become excreted in the urine per square inch of the surface covered).

Diagram 3.


Quantity applied to the skin.
100%
1 in 40.
Quantity absorbed by C.
2 hrs.
4 hrs.
6 hrs.
29.90%
48.03%
53.60%

Subject C. Table I.

Averages of 1 in 40 over 36, 72 & 108 sq. ins.

Time.	per cent.	per sq. in.	Total Phenol.	Ratio.
2 hours	28.90	5.02	361.34	1
4 hours	48.03	8.34	589.09	1.66
6 hours	53.60	9.31	654:61	1.85

In four hours time the corresponding numbers are 48.03% and 8.34 mgrs. per sq. in., showing a ratio of 1.66:1 as compared with those for 2 hours, i.e. ½ more, than was absorbed in the first 2 hours, becomes absorbed in 4 hours. Again, in 6 hours time there is only a slight increase over the amount for 4 hours, viz:- an everage of 53.6% and 9.31mgrs. per sq. in., a ratio as compared with 2 hours of 1.85:1 or ¾ more than was absorbed in 2 hours.

My general conclusion, with respect to the influence of time therefore is, that, roughly speaking, ½ more than was absorbed in 2 hours becomes absorbed in 4 hours; and that ¾ more becomes absorbed in 6 hours, than was absorbed in 2 hours (cf. diagram 3.)

I next consider the effect of increasing the extent of the skin surface. Thus, taking again a solution of 1 in 40 as before, I get, during the

three periods of time, an average absorption of 46.53 per cent or an average total excretion of 290.99 mgrs. over an area of 36 sq. in.

Subject C. Table 2.

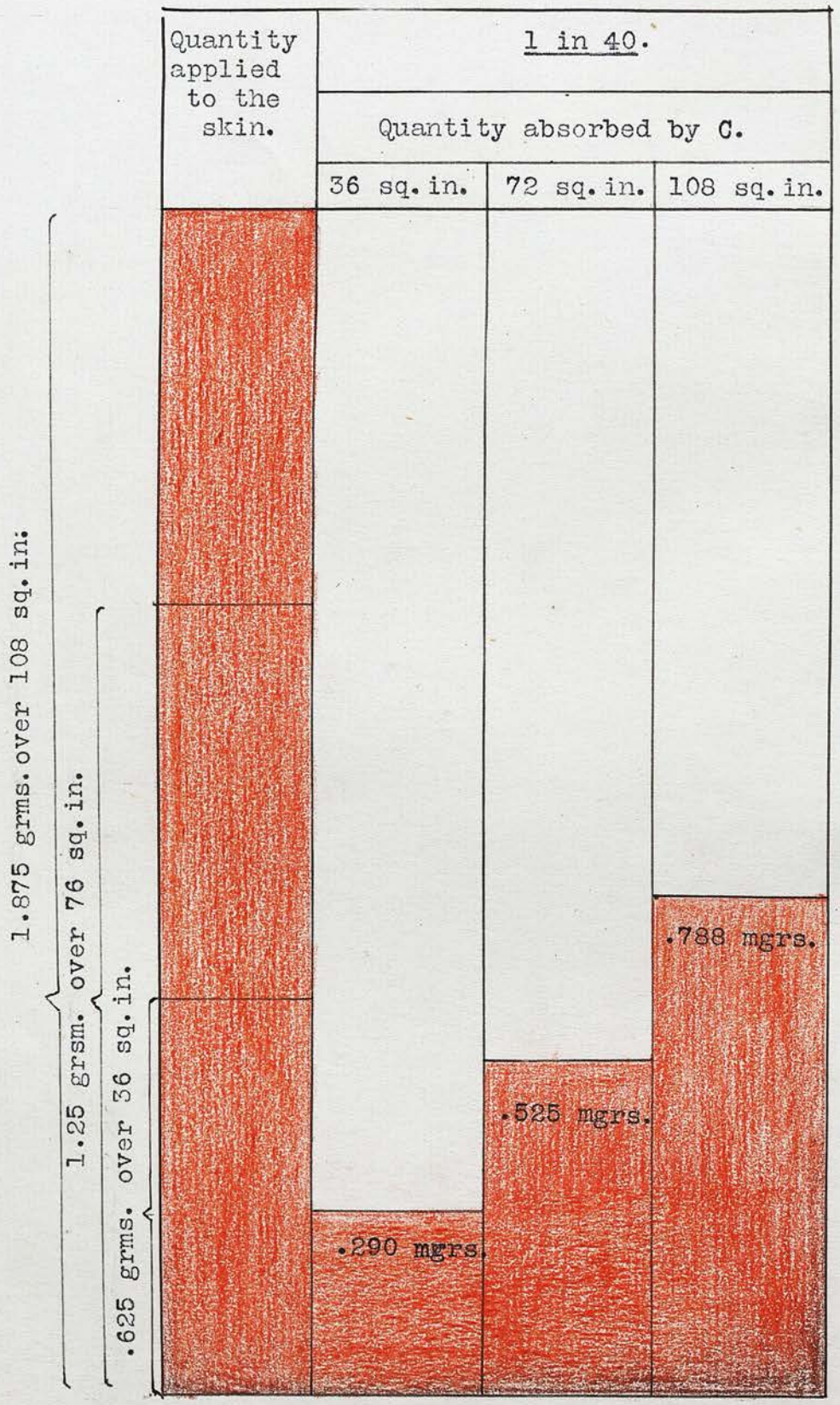
Averages of 1 in 40 for 2, 4 and 6 hours.

Surface.	per cent.	per sq. in.	Total Phenol	Ratio.
36 sq. ins.	46.53	8.07	290.99	1
72 sq. ins.	42.00	7.29	525.59	1.81
108 sq. ins.	42.00	7.29	788.45	2.71

If, without varying the duration of time, the poultice be now applied over twice that extent of surface, viz:- 72 sq. ins., there is an average percentage absorption of 42% or an average total absorption of 525.59 mgrs. Although there is a decrease in the percentage absorption of 1:902 yet there is an increased total absorption in the ratio of 1:1.81. In other words although there is relatively to the quantity of Phenol applied to the skin a smaller proportion of it absorbed, still there is an increased absorption of nearly ¾ more than was absorbed over 36 sq. ins.

I now treble the extent of surface, i.e. apply the Compress over 108 sq. ins., and I find that the average percentage absorption remains unchanged, al-

Diagram 4.


Quantity applied to the skin.
1 in 40.
Quantity absorbed by C.
36 sq. in.
72 sq. in.
108 sq. in.
1.875 grms. over 108 sq. in.
1.25 grsm. over 76 sq. in.
.625 grms. over 36 sq. in.
.290 mgrs.
.525 mgrs.
.788 mgrs.

though the average total absorption is considerably increased over that for 72 sq.ins., viz:- from 525.59 mgrs., to 788.45mgrs, or in a proportion of 1 : 2.71 as compared with that for 36 sq.ins., i.e., $1\frac{3}{4}$ more than was absorbed over 36 sq.ins.

Hence I conclude that, as the surface area is increased to twice and three times its original size, there is also a decided increase in the amount of Phenol absorbed, the ratios being 1, 1.81, and 2.71. It will be remembered that the doubling and trebling of the length of time gave ratios of 1, 1.66, and 1.85. So the influence of increasing the extent of skin surface is considerably greater than that of increasing the length of time of the application. (c.f. diagram 4.)

Let us now see the effect of a different strength of solution. Therefore instead of 1 in 40, I will take 1 in 80; and firstly, as before, I shall consider the influence of time. With this strength of solution applied over any surface, i.e., over any of the 3 surfaces with which I am dealing, there is an average absorption in 2 hours' time of 28.86% or 2.5 mgrs. per sq.in. (c.f. Table 3).

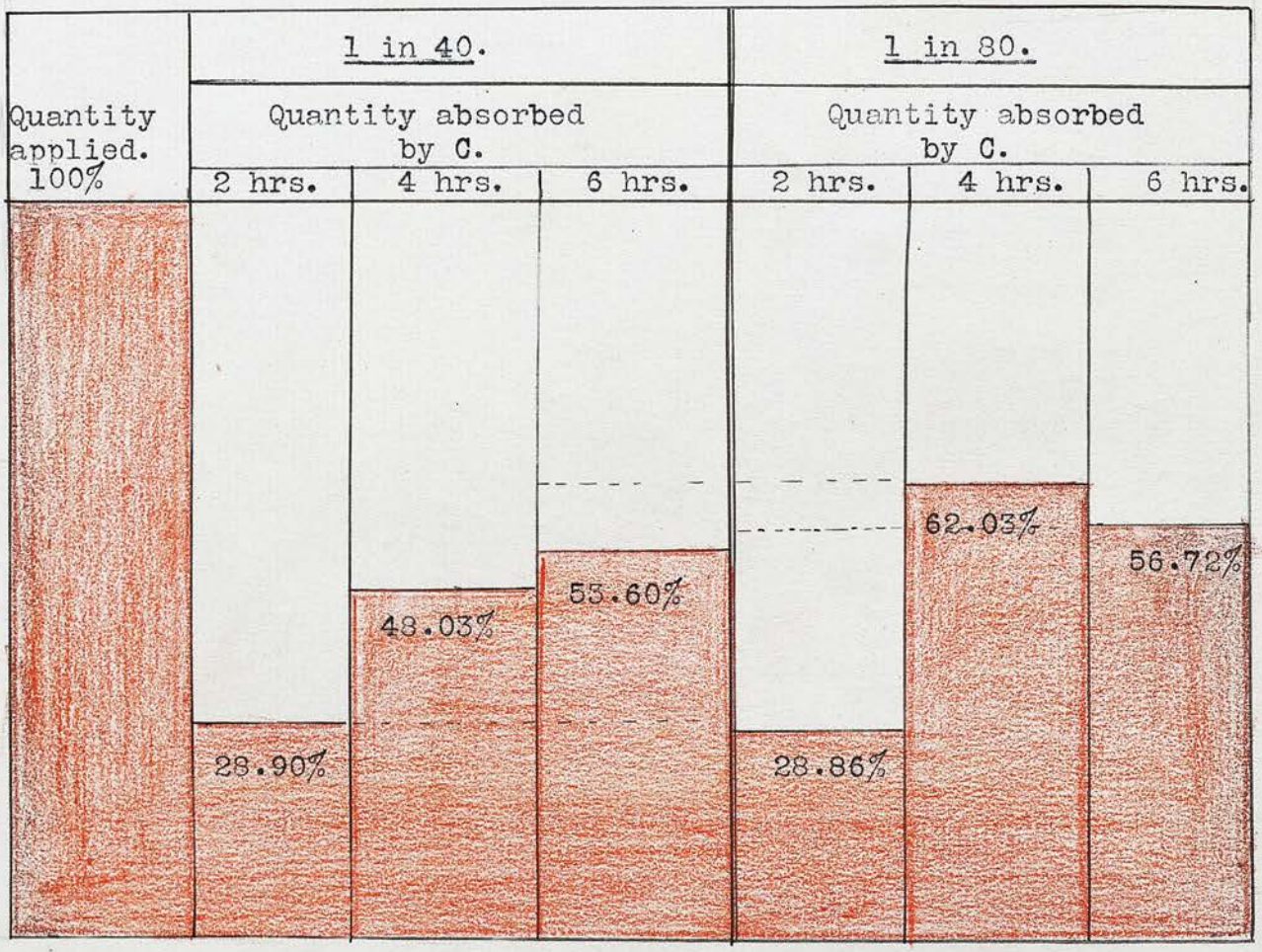
Subject C. Table 3.

Averages of 1 in 80 over 36, 72 & 108 sq. ins.

Time.	per cent.	per sq. in.	Total Phenol.	Ratio.
2 hours.	28.86	2.50	177.08	1
4 hours.	62.03	5.38	380.80	2.15
6 hours.	56.72	4.92	327.22	1.96

By doubling the length of time of application, i.e., leaving the compress on the skin for 4 hours, there is an average absorption of 62.03% or 5.38mgrs. per sq. ins., which is one and one seventh more than was absorbed in 2 hours' time, standing to it in the ratio of 2.15 : 1, and which is rather a remarkable result. In the case of the 1 in 40 solution, the ratio of absorption between the 4 and 2 hours' periods was less marked, being 1.66 : 1; and it is difficult to see why, with a weaker solution applied for twice the length of time more than twice the amount should be absorbed. Again, by increasing the length of time to 6 hours, the quantities absorbed are somewhat diminished, the average being 56.72% or 4.92 mgrs. per sq. in., and, as compared with that for 2 hours' time, stand to it in the ratio of 1.96 :1, while that for the 4 hours' period showed a proportion of 2.15 : 1, i.e., in 6 hours $\frac{19}{20}$ more becomes absorbed

Diagram 5.


1 in 40.
1 in 80.
Quantity applied. 100%
Quantity absorbed by C.
Quantity absorbed by C.
2 hrs.
4 hrs.
6 hrs.
2 hrs.
4 hrs.
6 hrs.
28.90%
48.03%
53.60%
28.86%
62.03%
56.72%

than was absorbed in 2 hours' time. Therefore in comparing this ratio of the weaker solution with the corresponding ratio of the stronger, it will be observed that the ratio between the 2 and 4 hours of the latter is somewhat less marked, being 1.85 : 1. So in conclusion I may state that, with respect to the influence of time in the 1 in 80 solution, there is absorbed in 4 hours $1\frac{1}{7}$ more than was absorbed in 2 hours, and that in the whole 6 hours' period $\frac{19}{20}$ more was absorbed than in 2 hours. (c.f. diagram 5.)

I shall next enquire how variation, in the extent of the surface, that is covered, alters the absorption of the quantity of Phenol in the weaker solution. By applying the compress over 36 sq.ins., there is an average percentage absorption of 54.46%, or an average total absorption of 170.20 mgrs. (c.f. Table4)

Subject C. Table 4.

Averages of 1 in 80 for 2, 4 and 6 hours.

Surface.	per cent.	per sq. in.	Total Phenol.	Ratio.
36 sq. ins.	54.46	4.72	170.20	1
72 sq. ins.	51.03	4.43	319.16	1.87
108 sq. ins.	42.13	3.66	395.74	2.32

If the poultice be now applied over double the extent of surface, viz:- over 72 sq.ins., and allowed to remain on for the same length of time, I find that there is an average absorption of 51.03% or an average total absorption of 319.16 mrgs. Notwithstanding that the ratio of the percentages is diminished by 1 : .937, yet the total absorption is increased by 1 : 1.87, i.e. over 72 sq.ins. $\frac{9}{10}$ more is absorbed than was absorbed over 36 sq. ins. When the extent of skin surface is increased to three times its original size, viz:- to 108 sq.ins., the proportion of the quantity absorbed is even yet more diminished as regrads the percentage absorption, viz:- 1 : .775. But according to the average total absorption of 395.74 mgrs., there is a considerably increased quantity absorbed in the ratio of 1 : 2.32, the ratio of increase, however being less marked than in the case of the 1 in 40 solution, which was 1 : 2.71. So it is seen, that according as the extent of surface is doubled or trebled, so there is an increased amount of Phenol absorbed in the respective ratios of 1, 1.87 and 2.32, which show an increase over those for double and treble the length of time respectively, these being 1, 2.15 and 1.96. So here as in the case of 1 in 40 solution, the influence of

Diagram 6.


Quantity applied to the skin.
1 in 40
Quantity absorbed by C.
36 sq. in.
72 sq. in.
108 sq. in.
1 in 80.
Quantity absorbed by C.
36 sq. in.
72 sq. in.
108 sq. in.
46.53%
.296 Grms.
42.00%
.525 Grms.
42.00%
.788 Grms.
54.46%
.170 Grms.
51.03%
.319 Grms.
42.13%
.395 Grms.

increasing the extent of skin surface is decidedly more marked than that of increasing the length of the time of the application, for, while over twice and three times the extent of surface $\frac{3}{4}$ and $1\frac{1}{2}$ times more is absorbed than over the original surface, there is in twice and three times the length of time only $\frac{1}{2}$ and $\frac{3}{4}$ more absorbed than was absorbed in 2 hours. (c.f. Diagram 6.).

Lastly I shall consider the effect of varying the strength of the solution, and this I do by comparing the results obtained by solutions of the strengths of 1 in 40 and 1 in 80 for corresponding periods of time and extents of surface. Firstly then, I shall compare them with respect to time. A priori, one would have no hesitation in saying that, in a solution of 1 in 40, double as much would be absorbed as in one of 1 in 80.

When the time is 2 hours, this is not quite the proportion; for instead of the ratio being 1 : 2, it is 1 : 1.99. In a 1 in 40 solution therefore, proportionally to the quantities applied, more becomes absorbed during the first 2 hours, than with 1 in 80. Referring to table 5 it will be noticed that the former stands to the latter in the proportion-

Subject C. Table 5.

Comparison of Averages of Time.

Time.	1 in 40			1 in 80			1 in 40 : 1 in 80.
	per cent.	per sq. in.	Total Phenol.	per cent.	per sq. in.	Total Phenol.	
2 hrs.	28.90	5.02	361.34	28.86	2.50	177.08	1 : .998
4 hrs.	48.03	8.34	589.09	62.03	5.38	380.80	1 :1.29
6 hrs.	53.60	9.30	654.61	56.72	4.92	327.22	1 :1.058

al ratio of 1 : .998, on the supposition that the quantities of Phenol applied are equalised in the two cases. Or again in Experments 15 and 91 C or Table (8) (PAGE 71A) where in the one case 50 c.c. of 1 in 80 solution, and in the other 25 c.c. of 1 in 40 solution, i.e., equal quantities were applied respectively over areas of 72 sq.ins., and 36 sq.ins., it will be noticed that the percentage absorption of the latter is 29.3%, while for the former it is 27.5%, i.e., again very little more is absorbed from the 1 in 40 solution than from the 1 in 80. How this is brought about is difficult to explain. Might the stronger solution, by being more quickly absorbed, not have injured the skin tissues to such an extent, as to interfere with absorption during the rest of the time? This seems to me to be the only feasible explanation.

Although this is the case for 2 hours, I find that the proportion is reversed, when the duration of the time of application is doubled, the ratios now standing as 1 : 1.29. This is again borne out by experiments 19 and 96 C, or Table 8. Where 25 c.c. of 1 in 40 over 36 sq.ins. and 50 c.c. of 1 in 80 over 72 sq.ins. respectively, i.e. equal quantities, yielded 50.9% and 67.5%. When the poultice is allowed to remain on the skin for a greater length of time, as for 6 hours, the absorption from the 1 in 80 solutions is still slightly in an increased ratio, being now 1 : 1.058. The results of experiments 23 and 101 C, or Table 8. with 25 c.c. of 1 in 40, and 50c.c. of 1 in 80 are very nearly equal, being 59.4% and 58.0% respectively.(cf.Diag.5 p.65)

The strong and weak solutions now fall to be considered in their space relations. As before, one would again expect that double as much would be absorbed in the case of the 1 in 40 solution as in the 1 in 80; but again a divergence from this is noticed. From Table 6 it can be inferred that, by the application of 1 in 80 solutions over 36 sq.ins. of skin surface more is relatively absorbed than by that of 1 in 40, the proportional

ratio being 1.17 : 1. When applied over twice this extent of skin surface, viz:- 72 sq.ins., there is even a greater relative increase with the 1 in 80 solution than before, viz:- 1.215 : 1.(cf.Diagram 6,p.67)

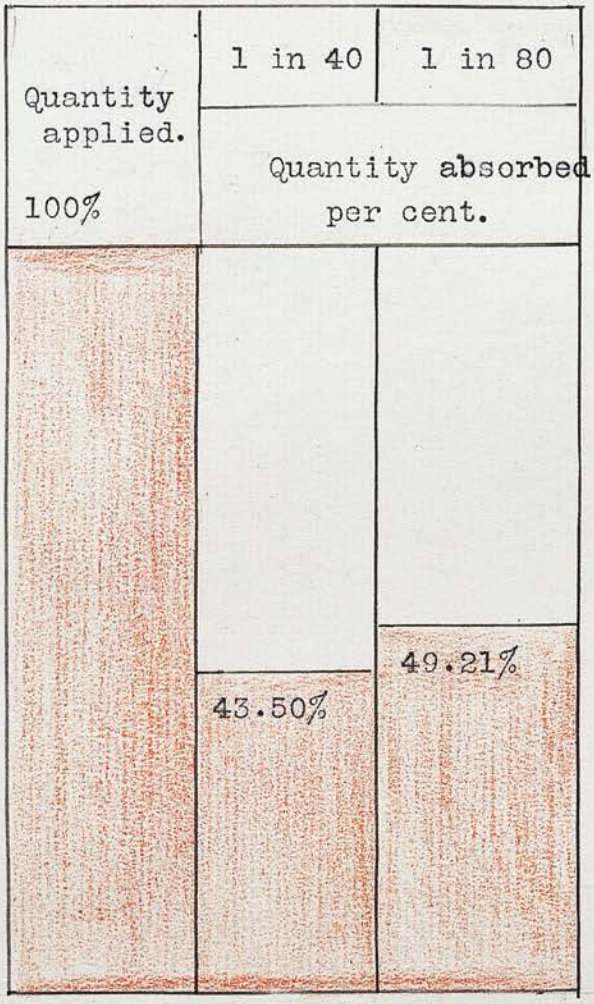
Subject C. Table 6.

Comparison of Averages of Surface.

Surface.	1 in 40			1 in 80			
	per cent.	sq.ins.	Total.	per cent.	sq.ins.	Total.	1 in 40:1 in 80
36 sq.ins.	46.53	8.07	290.99	54.46	4.72	170.20	1 : 1.170.
72 " "	42.00	7.29	525.59	51.03	4.43	319.16	1 : 1.215
108 " "	42.00	7.29	788.45	42.13	3.66	395.74	1 : 1.003

And lastly, when the area is increased to three times its extent, it is noticed that while the ratio is less marked, it is still in favour of the 1 in 80 solution. It will thus be seen that the only instance, where proportionally more is absorbed from the application of a 1 in 40 solution than from that of 1 in 80 is during the first 2 hours over any of the three areas; but thereafter the balance continues in favour of the more dilute solution. I find that the greatest difference in the proportional absorption between the stronger and the weaker solutions is during the 4 hours' period, and when applied over an area of 72 sq.ins. (Tables 5 & 6).

Diagram 6a.


Quantity applied.
100%
1 in 40
1 in 80
Quantity absorbed per cent.
43.50%
49.21%

As the surface is increased and as the time is lengthened beyond 4 hours, so the proportional ratio tends to become equalised.

Therefore in conclusion, I may state that, on the whole, as will be readily seen by referring to table 7, the weaker solution is relatively more quickly absorbed than the stronger in the ratio of 1.13 : 1.; of course, with respect to the actual or absolute amount absorbed, the case stands quite differently, very nearly double being absorbed from 1 in 40 as compared with 1 in 80. (c.f. Diagram 6a.)

Subject C. Table 7.

Comparison of Grand Averages for 2, 4 & 6 hours over 36, 72 and 108 sq. ins.

	per cent.	per sq. in.	Total.	Proportional Rat.
1 in 40	43.50	7.55	535.01	1
1 in 80	49.21	4.27	295.04	1.13

Table 8.

	25 cc. 1 in 40 (.625 mgrms. Phenol over 36 sq. in.			50 cc. 1 in 80 (.625 mgrms. Phenol) over 72 sq. in.			Ratio for Adults.	
	A. %	B. %	C. %	A. %	B. %	C. %	1 in 40 over 36 sq. inches.	1 in 80 over 72 sq. inches.
2 hrs. Expts.	13	14	15	89	90	91		
	28.3	29.3	29.3	26.3	18.6	27.5	1	: .833
4 hrs. Expts.	17	18	19	94	95	96		
	29.9	41.9	50.9	34.7	63.4	67.5	1	: 1.349
6 hrs. Expts.	21	22	23	99	100	101		
	63.8	35.5	59.4	60.9	31.5	58.0	1.	: 1.947
Total average percentage of time.	40.66	34.90	46.53	40.63	37.83	51.00		
Average percentage for all adults.	40.70 (adults)			43.15 (adults)			1	: 1.06

PART II.

Average results of Experiments with 3 adults.

Having considered the case of a single individual, in whom the process of absorption was fairly uniform, and thus obtained a general conception as to the influence of time and extent of skin surface covered in modifying the amount excreted in the urine, I shall now take a view of the averages of 3 adults A, B and C and see how far the results correspond with those of the single individual; because, as will be seen later on individuality counts for much in this matter. With reference to the question of how much on an average is absorbed by an adult from a certain strength of solution applied to a skin surface I find that with a 1 in 40 solution as much as 26.5 per cent of the amount applied to the skin or 4.60 mgrs per square inch of surface covered becomes excreted in the urine, when the application was made over a period of 2 hours,

Adults Averages of 1 in 40 Table 9.
Table 9. over 36, 72, & 108 sq. ins.

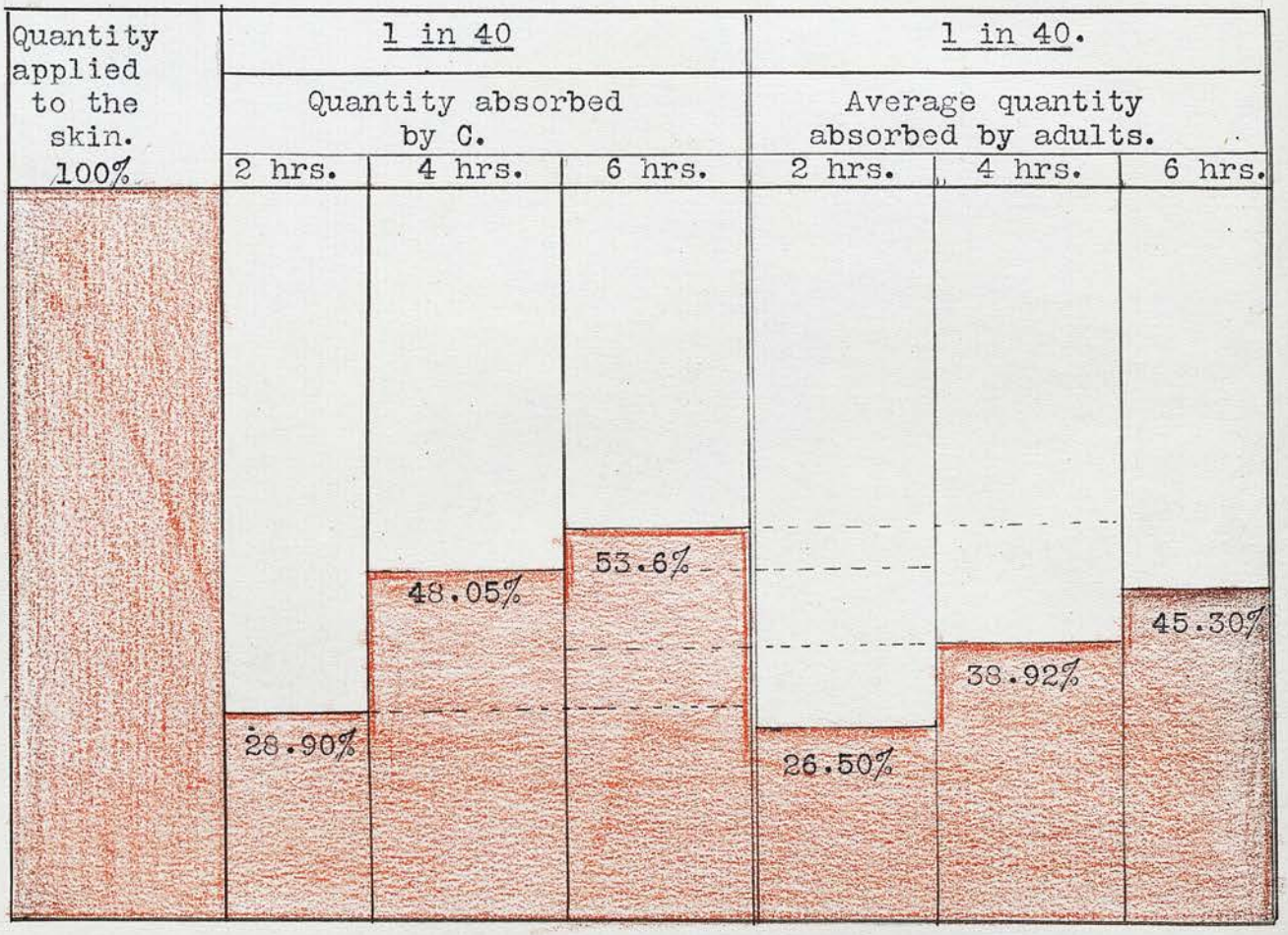
Time	per cent	per sq. in.	Total Phenol.	Ratio
2 hrs.	26.50	4.60	304.93	1
4 "	38.92	6.75	483.75	1.586
6 "	45.30	7.86	538.08	1.764

while these are the averages, there is a variation

among different individuals ranging from 20.4 per cent to 29.3 per cent. In order to study the effect of time in modifying absorption, I leave the poultice applied for twice the length of time, viz. for 4 hours, and it might be expected, that also twice the amount would be absorbed; but this does not occur. The averages obtained viz. 38.92 per cent or 6.75 mgrs. per sq. in. stand to those for the 2 hours' period in the ratio of 1.58:1 instead of the time ratio 2:1. That is that practically only ½ more is absorbed in 4 hours than was absorbed in 2 hours. When the length of time of the application is still further increased to 6 hours the amount of phenol absorbed shows only a slight increase over that of the 4 hours' period, the averages now being 45.30 per cent or 7.86 per sq. in. and bearing a ratio to that for the two hours' period of 1.764:1 or about ¾ more than was absorbed in 2 hours.

This is probably to be accounted for by there being less phenol left in contact with the skin to be absorbed during the last 2 hours of the 6; and perhaps also because there being more phenol on the other side of the skin septum, the rate of defusion is less, assuming that the absorption takes place in this manner.

Diagram 7.


Quantity applied to the skin.
100%
1 in 40
Quantity absorbed by C.
2 hrs.
4 hrs.
6 hrs.
1 in 40.
Average quantity absorbed by adults.
2 hrs.
4 hrs.
6 hrs.
28.90%
48.05%
53.6%
26.50%
38.92%
45.30%

When these results are compared with the corresponding ones of the individual case C, (Table I) it will be noticed that they are very nearly the same (cf. Diagram 7)).

Having considered the effects of the variation of the length of the time, I shall now, as was done in subject C, again enquire how far extent of surface may influence the amount excreted. This I do by proportioning the amount of phenol in the poultice to the extent of skin surface covered i.e., when I increase the extent of surface to twice and three times its original size, I likewise double or treble the amount of phenol applied. Just as in the case of multiplying the time of application we found that the absorption was not multiplied in the same ratio, so here with respect to the extent of surface covered , we observed something similar. We should naturally expect double the extent of skin surface to afford a double absorption; but this is not what actually takes place, although there is a nearer approach to the space ratio than there was to that of the time. Thus irrespective of time, I find that the average absorption of the adult over 36 sq. in. (255.90 mgrs.) as compared with that over 72 sq. in. (436.62 mgrs.) is in the

proportion of 1:1.70 (Table 10) instead of the space ratio 1;2.

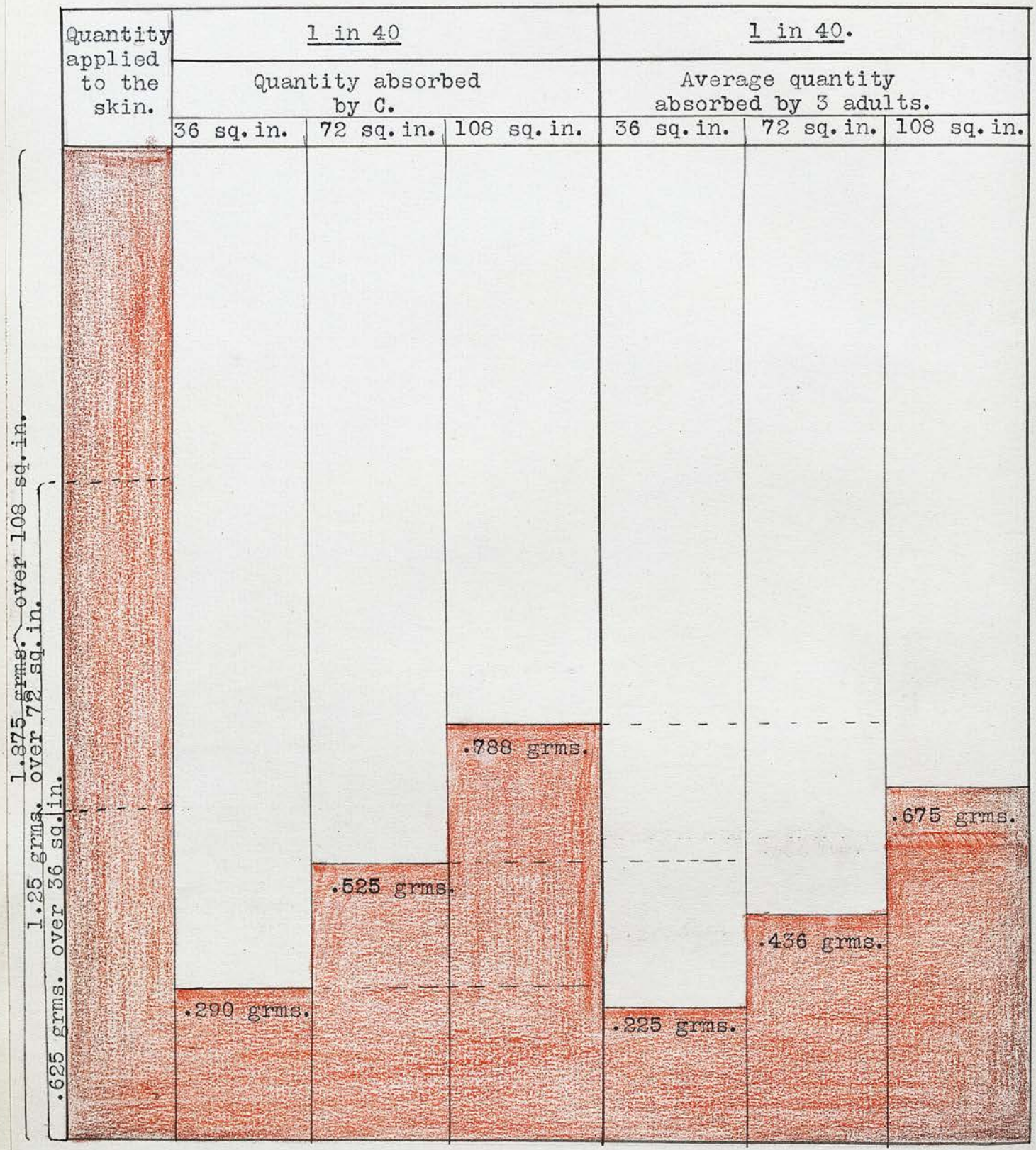
Adults — Averages of 1 in 40
Table 10. — For 2, 4, & 6 hours.

Surface	per cent	per sq. in.	Total Phenol.	Ratio.
36 sq. in.	40.92	7.10	255.90	1
72 "	34.88	6.06	436.62	1.70
108 "	35.97	6.25	675.41	2.64

It is therefore seen that the percentage absorption is somewhat diminished from 40.92 to 34.88 per cent, but yet $\frac{3}{4}$ more is absorbed than from 36 sq. ins.

If the extent of surface be increased to three times its former size viz. 108 sq. ins., I find that the average percentage absorption is very much the same as with 72 sq. ins., while the average total quantity of phenol excreted is considerably increased viz. from 436.62 mgrs to 675.41 mgrs or in the proportion of 1:2.64 as compared with that for 36 sq. ins. In other words although there is relatively to the quantity of phenol applied to the skin a smaller proportion absorbed as the poultice is applied over twice and three times the surface, still there is absorbed nearly $\frac{3}{4}$ and $1\frac{1}{2}$ times more than was absorbed from the original area. And if (Table 2) be again consulted it will be seen that in the case of subject C, similar results were obtained. Hence it is seen that there is a proport-

Diagram 8.


Quantity applied to the skin.
1 in 40
Quantity absorbed by C.
36 sq. in.
72 sq. in.
108 sq. in.
1 in 40.
Average quantity absorbed by 3 adults.
36 sq. in.
72 sq. in.
108 sq. in.
1.875 grms. over 108 sq. in.
1.25 grms. over 72 sq. in.
.625 grms. over 36 sq. in.
.290 grms.
.525 grms.
.788 grms.
.225 grms.
.436 grms.
.675 grms.

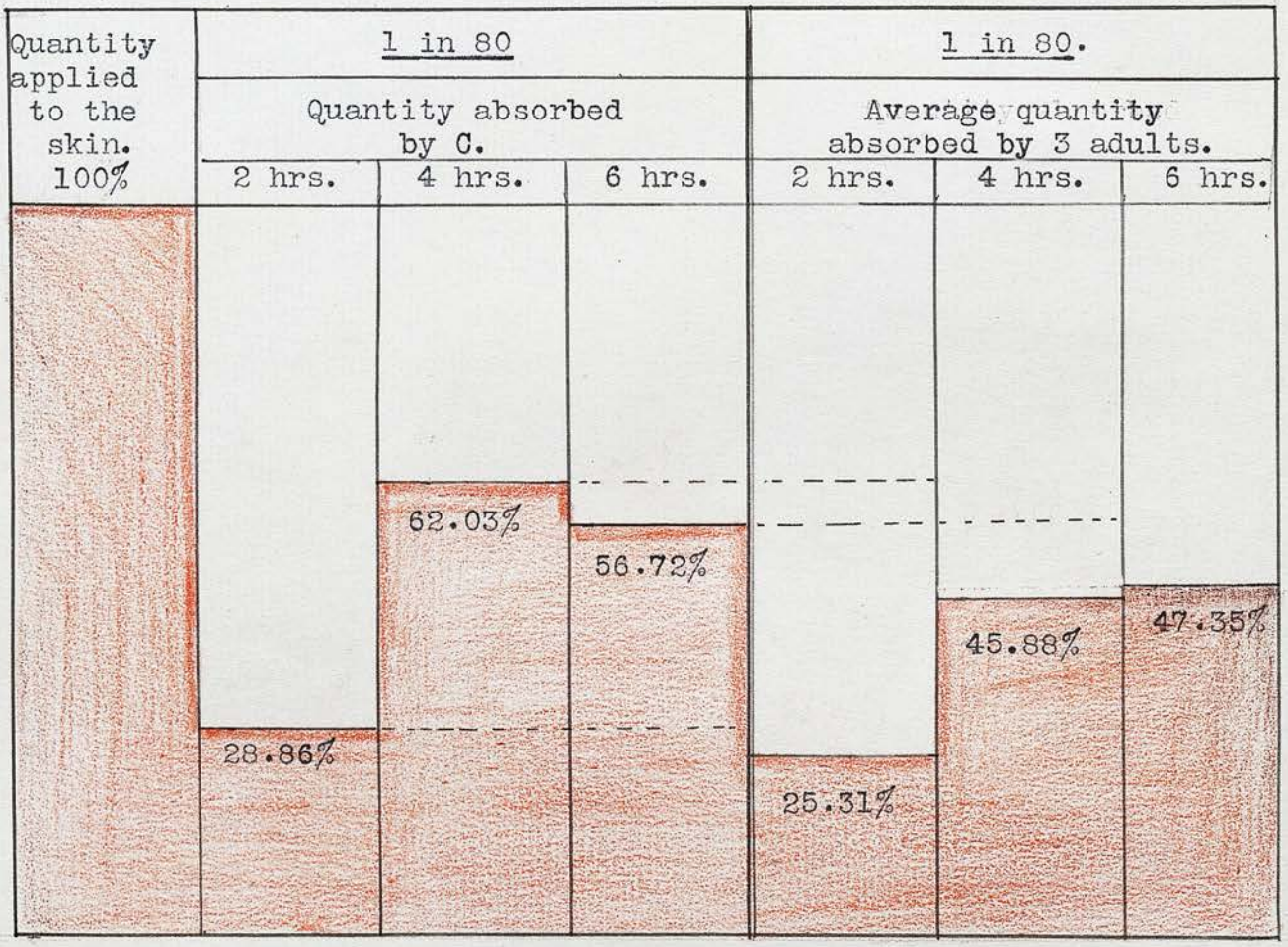
ionally less absorption, according as the absorbing area is increased, probably because the balance on the other side of the septum is sooner reached, owing to greater quantities entering. And it will be remembered that in twice and three times the length of time I obtained ratios of 1, 1.586 and 1.764. So I can definitely state that the influence of increasing the extent of skin surface affects the absorption more markedly than that of increasing the length of time of the application. (cf. diagram 8) Let us now take a weaker solution such as 1 in 80 instead of 1 in 40, in order to see how it behaves with respect to variations in the length of time of the application and in the extent of surface covered; and firstly I will consider it with respect to time. With this strength of solution applied over any of the three surfaces there is an average absorption in 2 hours' time of 25.31 per cent or 2.19 mgrs per sq. in. (Table 11)

Adults
Table 11.

Averages of 1 in 80
over 36, 72 & 108 sq. in.

Time	per cent	per sq. in.	Total Phenol.	Ratio
2 hrs.	25.31	2.19	159.65	1
4 "	45.88	3.98	286.73	1.80
6 "	47.35	4.11	279.35	1.87

Diagram 9.


Quantity applied to the skin. 100%
1 in 80
Quantity absorbed by C.
2 hrs.
4 hrs.
6 hrs.
28.86%
62.03%
56.72%
1 in 80.
Average quantity absorbed by 3 adults.
2 hrs.
4 hrs.
6 hrs.
25.31%
45.88%
47.35%

In double the length of the time of application, i.e. leaving the compress in contact with the skin for 4 hours, there is an average absorption of 45.88 per cent of the amount applied or 3.98 mgrs. per sq. in., which is about $\frac{3}{4}$ more than was absorbed in 2 hours, standing to it in the ratio of 1.80:1. Again by increasing the length of time to 6 hours the quantities of Phenol are only slightly increased over those for 4 hours, namely 47.53 per cent or 4.11 mgrs. per sq. in., and as compared with those for 2 hours' time stand to them in the proportion 1.87:1, while those for the 4 hours' period showed a proportion of 1.80:1 i.e. in the whole 6 hours about 7/8 more is absorbed than in 2 hours. Therefore in comparing this ratio of the weaker solution with the corresponding ratio of the stronger it will be observed that the ratio of the 1 in 40 solution is somewhat less marked being 1.764:1. (cf. Diagram 9.) And although the typical subject C gave practically the same ratio for 2 and 6 hours he showed a very much more marked ratio for the 4 hours viz. 2.15:1. Anomalies such as these, I can only explain by the well ascertained fact, to be dealt with later on, that the absorptive activity of the skin varies very much even in the same individuals on different occasions. So in conclusion I may state

that, with respect to the influence of time in the 1 in 80 solution there is absorbed in 4 hours $\frac{3}{4}$ more than was absorbed in 2 hours, and that in 6 hours 7/8 more is absorbed than was absorbed in 2 hours, which is about the same result that was obtained with the stronger solution of 1 in 40.

My next enquiry will be how variation in the space covered, affects the quantity absorbed in the 1 in 80 solution. By applying the compress over 36 sq. ins., the average total absorption for the day is 125.82 mgrs or 40.26 per cent of the amount applied (Table 12).

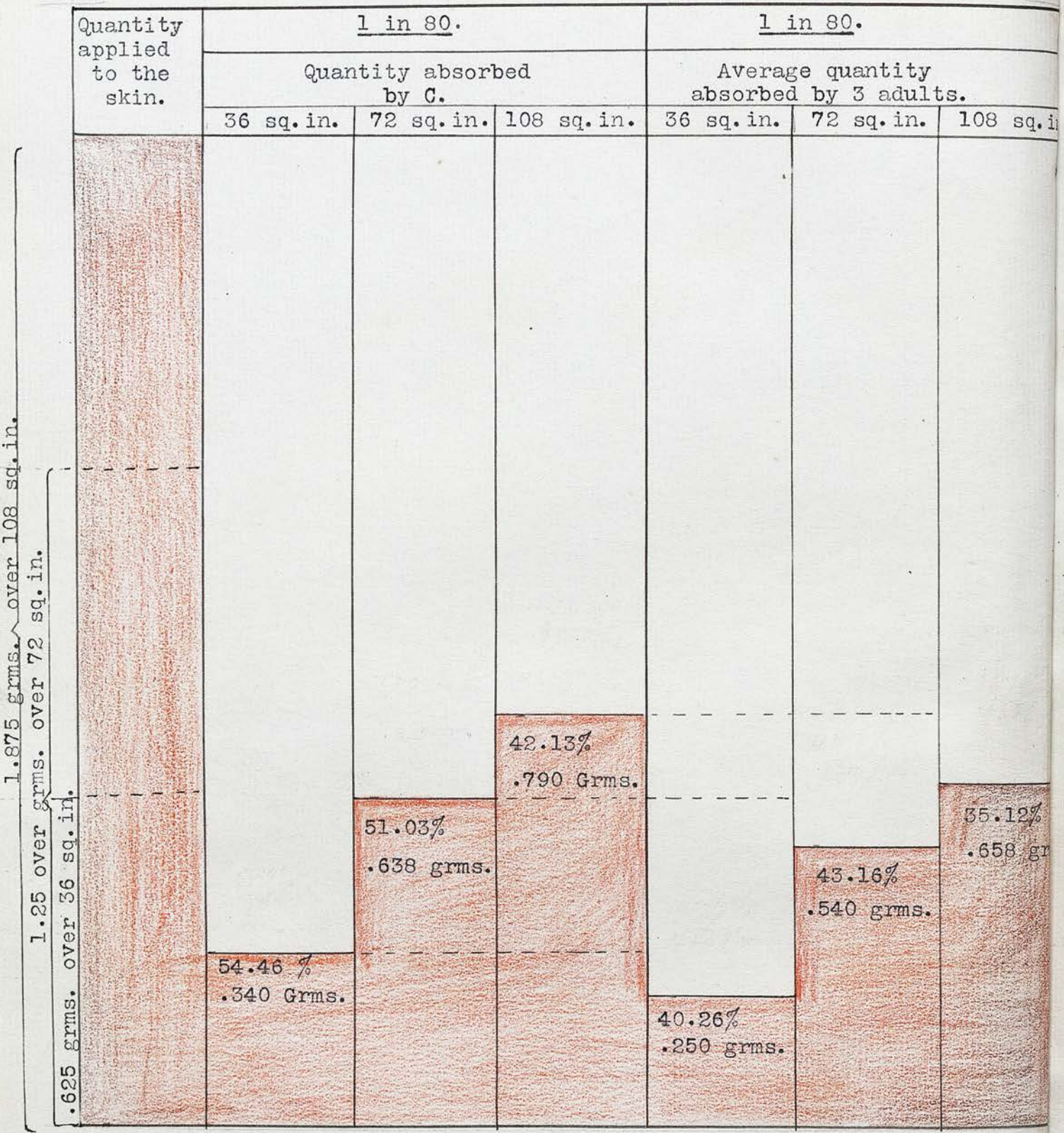
Adults. Table 12.

Averages of 1-80 for 2, 4 & 6 hours.

Surface	per cent	per sq. in.	Total Phenol.	Ratio.
36 Sq. in.	40.26	3.49	125.82	1
72 "	43.16	3.74	270.10	2.15
108 "	35.12	3.05	329.79	2.62.

On the other hand, if the poultice be again applied over twice the extent of surface viz. 72 sq. ins., and be allowed to remain on the skin for the same length of time, the average total absorption within 24 hours amounts to 270.10 mgrs. or a percentage of 43.16; i.e. over 72 sq. ins. about $1\frac{1}{6}$ more is absorbed than when 36 sq. ins. were covered, the ratio being 2.15:1. This is more than the corresponding amount which was

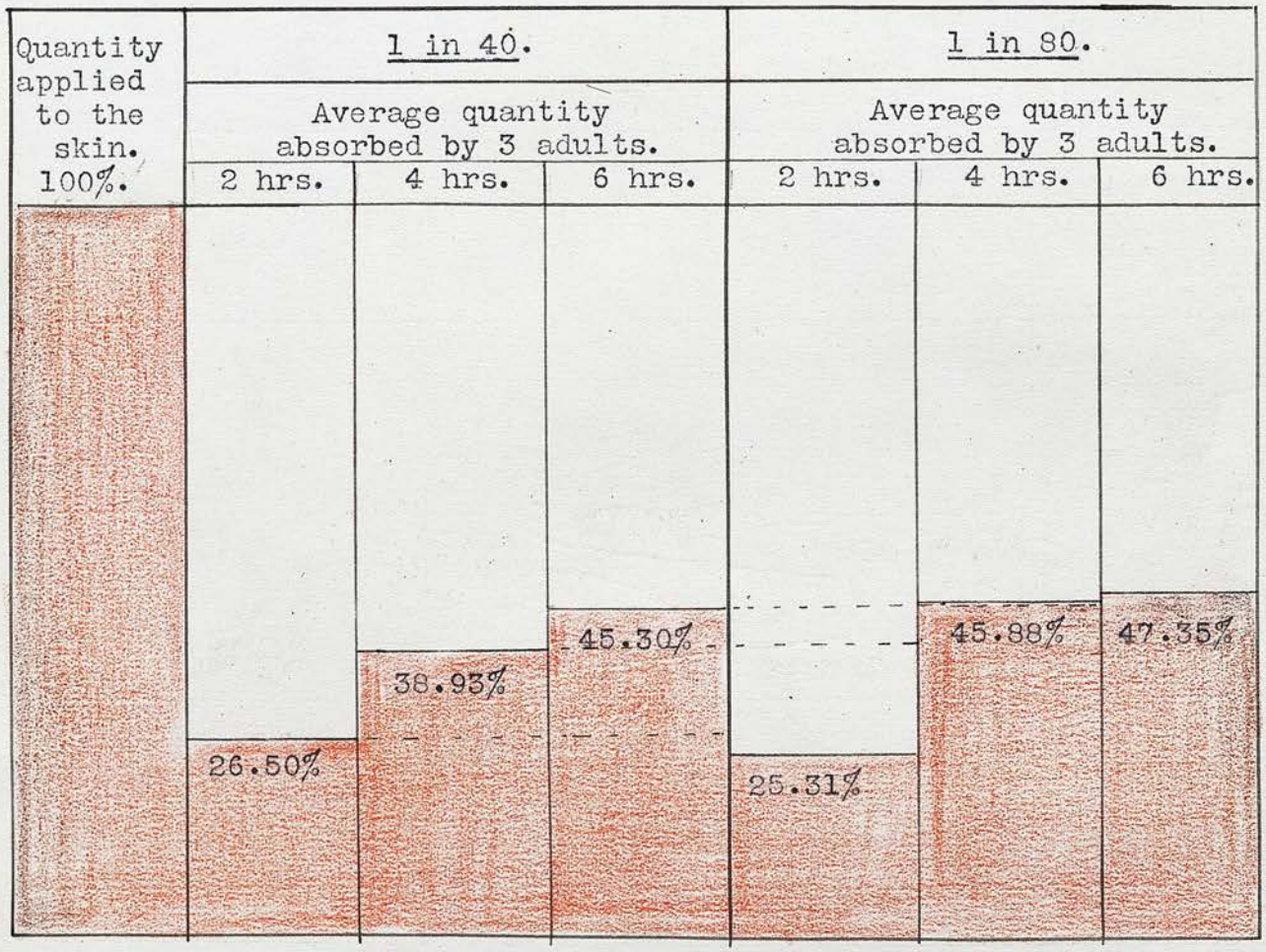
Diagram 10.


Quantity applied to the skin.
1 in 80.
Quantity absorbed by C.
36 sq. in.
72 sq. in.
108 sq. in.
1 in 80.
Average quantity absorbed by 3 adults.
36 sq. in.
72 sq. in.
108 sq. i
1.875 grms. over 108 sq. in.
1.25 over grms. over 72 sq. in.
.625 grms. over 36 sq. in.
54.46 %
.340 Grms.
51.03%
.638 grms.
42.13%
.790 Grms.
40.26%
.250 grms.
43.16%
.540 grms.
35.12%
.658 gr

absorbed by C (viz. 1:1.87). Notwithstanding that the ratio of the percentages is only increased by 1:1.07 yet the total absorption is increased by 1:2.15. When the extent of skin surface is increased to three times its original size viz. to 108 sq. ins., the proportion of the quantity absorbed to the quantity applied is somewhat less than it was for 72 sq. ins. being 35.12 per cent or in the ratio of .874:1 as compared with 36 sq. ins. But, even though that be so, according to the average total absorption of 329.79 mgrs, there is a considerable increased quantity absorbed in the ratio of 1:2.62; or nearly 1½ times more is absorbed over 108 sq. ins. than when applied over 36 sq. ins., the rate of increase being exactly the same as was noticed in the case of the 1 in 40 solution which was 1:2.64, and slightly more marked than in Subject C (1:2.32). (cf. diagram 10.)

So it is seen that according as the extent of surface is doubled or trebled there is also an increased amount of Phenol absorbed in the respective ratios of 1, 1.70 and 2.64 for 1 in 40 solution; and 1,2.15, and 2.62 for 1 in 80 solution, which shows a great increase over that for double and treble the length of time respectively, these being 1,1.58 and 1.76 for the 1 in 40 solution and 1,1.80, and 1.87 for the 1 in 80 solution.

Diagram 11.


Quantity applied to the skin. 100%.
1 in 40.
Average quantity absorbed by 3 adults.
2 hrs.
4 hrs.
6 hrs.
1 in 80.
Average quantity absorbed by 3 adults.
2 hrs.
4 hrs.
6 hrs.
26.50%
38.93%
45.30%
25.31%
45.88%
47.35%

I therefore can conclude that with all adults the influence of increasing the extent of skin surface is very much greater than that of increasing the length of time of the application. For, while by increasing the surface to 72and 108 sq.ins. ¾ and 1½ times more is respectively absorbed than for 36 sq.ins., by increasing the time to 4and 6 hours, only ½ and ¾ times more is respectively absorbed than was absorbed for 2 hours. Finally a comparison is instituted in a two-fold manner between the two different strengths of solution to ascertain their effects when applied to the same extent of skin surface, and for the same length of time. Firstly then I shall compare them with respect to time, (Table 13) (cf. Diagram 11)

Adults

Table 13.

Comparison of Averages of time.

	1 in 40			1 in 80			
Time	per cent	per sq. in.	Total Phenol.	Per cent	Per sq. in	Total Phenol	1 in 40:1 in 80.
2 hrs.	26.50	4.60	304.93	25.31	2.19	159.65	1 : 95
4 "	38.92	6.75	483.75	45.886	3.98	286.73	1 : 1.18
6 "	45.30	7.86	538.08	47.35	4.11	179.33	1 : 1.04

It will be remembered that in subject C. proportionally more was excreted with the 1 in 40 solution during the first 2 hours than with the 1in 80 solution, but that during the 4 and 6 hours' periods the quantities excreted by 1in 80 solution predominated over those for 1in 40.

So here too it will be noticed that during the first 2 hours the stronger solution stands to the weaker in the proportional ratio of 1: .95, that is to say, relatively to their strengths more becomes excreted during the first 2 hours from the application of 1 in 40 solutions than from the 1 in 80 solutions (Table 13) or that, if a certain amount is absorbed within 2 hours from a solution applied over an area, less will be absorbed when the strength of the solution is doubled and then applied over half the extent of surface (cf. experiments 17,18,19,94,95 & 96 Table 28.-: or Table 8, p.71a). This, it will be seen, I illustrated by applying on the one hand 25 c.c. of 1 in 40 solution over 36 sq. ins., and 50 c.c. of 1 in 80 solution over 72 sq. ins., on the other hand. But as before by applying the poultice for twice and three times the length of time, I find, that the proportion absorbed from these two solutions relatively to their strengths, is reversed and that now the 1 in 80 solution applied for periods of 4 and 6 hours shows respective ratios of 1.18:1 and 1.04:1 to the 1 in 40 solution. This proportion is again borne out by experiments 21,22,23,99,100,101 Table 28 (cf. Table 8) where 25 c.c. of the 1 in 40 solution were applied over 36 sq. ins., and 50 c.c. of the 1 in 80 solution over 72 sq. ins. The probable explanation

for this is the same as that given for C viz. that the 1 in 40 solution, being stronger and more quickly absorbed, injures the tissues of the skin to such an extent, that absorption is somewhat interfered with during the rest of the time. Therefore, as regards time, it is seen that the only difference of any consequence between the relative quantities absorbed by these two solutions is, that during the 4 hours' period the absorptive action, relatively to the amount applied, of the 1 in 80 solution is considerably stronger than that of the 1 in 40 solution; and practically the same was observed in the typical subject C. When the two solutions are compared with respect to the extent of surface covered it is observed that the amount absorbed from the 1 in 40 solution applied over 36 sq. ins., stands to that of the 1 in 80 in the proportion of 1: .98, more being relatively absorbed from the 1 in 40 solution than from the 1 in 80 solution probably because of the 1 in 40 solution being more quickly absorbed during the first 2 hours. (cf. Table 14)

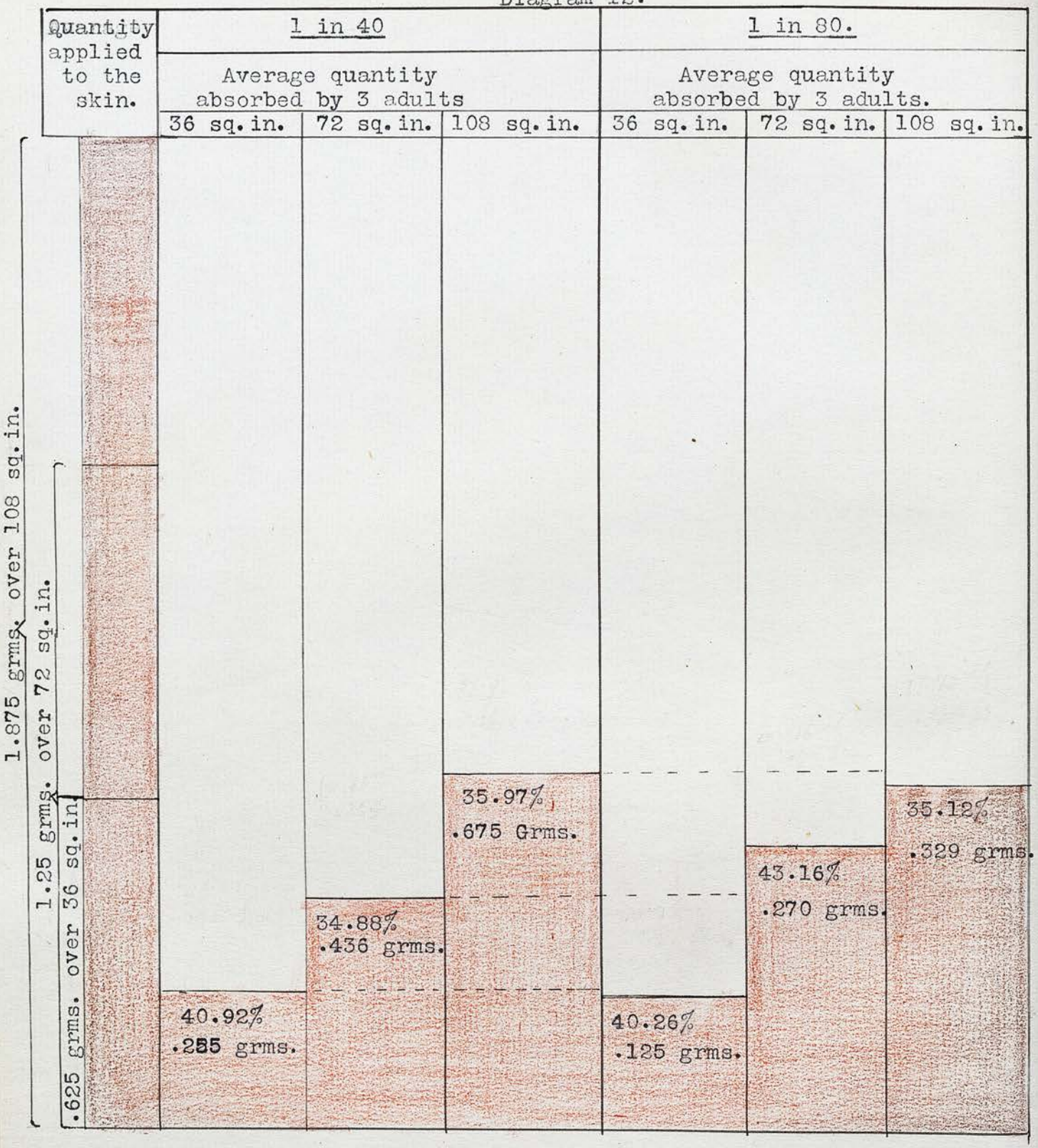
Adults

Table 14

Comparison of Averages of Surface.

	1 in 40			1 in 80			
Surface	per cent	per sq. in.	Total Phenol	per cent	per sq. in.	Total Phenol	1in40: 1in80
36 sq. in	40.92	7.10	255.90	40.26	3.49	125.82	1 : .98
72 "	34.88	6.06	436.62	43.16	3.74	270.10	1 : 1.23
108 "	35.97	6.25	675.41	35.12	3.05	329.79	1 : .97

Diagram 12.


Quantity applied to the skin.
1 in 40
Average quantity absorbed by 3 adults
36 sq. in.
72 sq. in.
108 sq. in.
1 in 80.
Average quantity absorbed by 3 adults.
36 sq. in.
72 sq. in.
108 sq. in.
1.875 grms. over 108 sq. in.
1.25 grms. over 72 sq. in.
.625 grms. over 36 sq. in.
40.92%
.255 grms.
34.88%
.436 grms.
35.97%
.675 Grms.
40.26%
.125 grms.
43.16%
.270 grms.
35.12%
.329 grms.

When applied over double the surface there is a relative increase of 8.28 per cent in the percentage absorption of the 1 in 80 solution; whereas, when applied over three times the extent of surface the percentage absorption of the 1 in 40 and 1 in 80 solutions are nearly the same, being respectively 35.97 per cent and 35.12 per cent, or very much in the same proportion as with subject C who had 42.00 per cent and 42.13 per cent. (cf. Diagram 12.)

It will thus be seen from these data that again the only instance where, proportionally to their strength, more is absorbed from the application of a 1 in 40 solution than from that of 1 in 80 is during the first 2 hours over any of the three areas; but that the weaker solution prevails over the stronger during periods of 4 and 6 hours in the relative amount of Phenol absorbed. I also found again that the greatest difference in the proportional absorption between these two solutions is during 4 hours and when applied over an area of 72 sq. ins., but I can state that for all practical purposes the absorption may be considered equal in the two solutions during periods of 2 and 6 hours and when applied over 36 and 108 sq. ins.

So in conclusion, by comparing the averages over the three areas and during the three periods of the

two solutions, I find that the weaker solution is only to a slight degree more quickly absorbed than the stronger, the percentage ratio of absorption being 1.06:1 (cf. Table 15) (cf. Diagrams 12 & 13.)

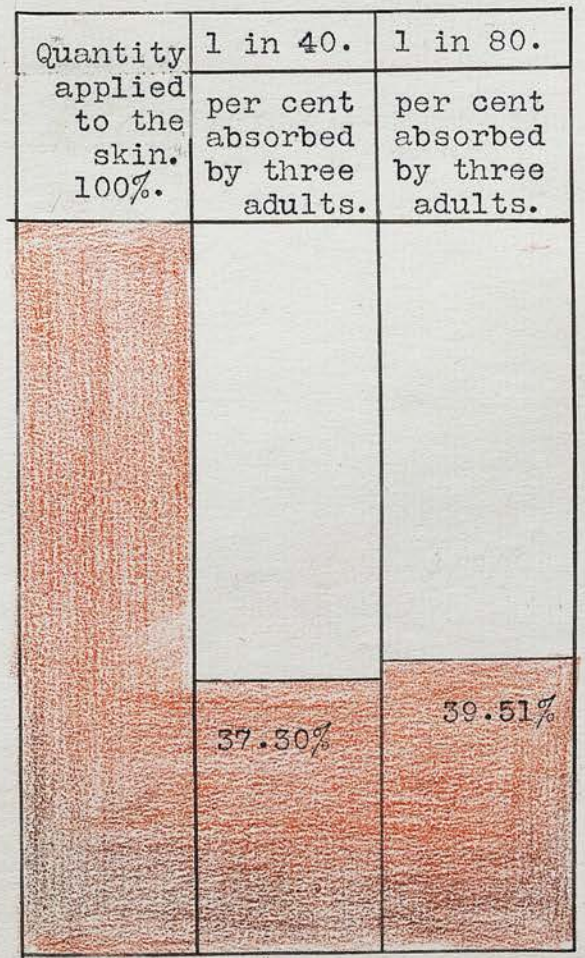
Adults

Table 15.

Comparison of grand averages for 2,4,& 6 hours over 36,72 & 108 sq. inches.

Strength	per cent	per sq. in.	Total Phenol	Ratio
1 in 40	37.30	6.47	447.53	1
1 in 80	39.51	3.42	241.90	1.06

Diagram 13.



AVERAGE RESULTS OF EXPERIMENTS WITH THREE CHILDREN.

So far as I have gone hitherto, I have been dealing only with the skin of adults; but owing to the greater number of deaths from poisoning by Phenol having occurred among children, and also owing to the experience that children are more liable to be affected by the absorption of Carbolic Acid, it becomes an important matter to know exactly how this peculiarity arises.

For this purpose, therefore, I shall fully discuss the rate of absorption as regards time, extent of skin surface and strength of solution in the more delicate skin of the child; and subsequently compare the results with what happens in the adult.

Firstly, then, to consider the influence of time, I shall begin with the 1 in 40 solution. When this is applied over any of the three areas for a period of two hours, I get an average percentage absorption of 41.28 per cent, or a total absorption of 537.67 mgrs. (cf. Table 16.)

While this is taken as an average, there is a considerable variation as to the quantity absorbed among the diffierent children, ranging from 24.2 per cent to 55.8 per cent. (cf. Table 16.)

Children Table 16

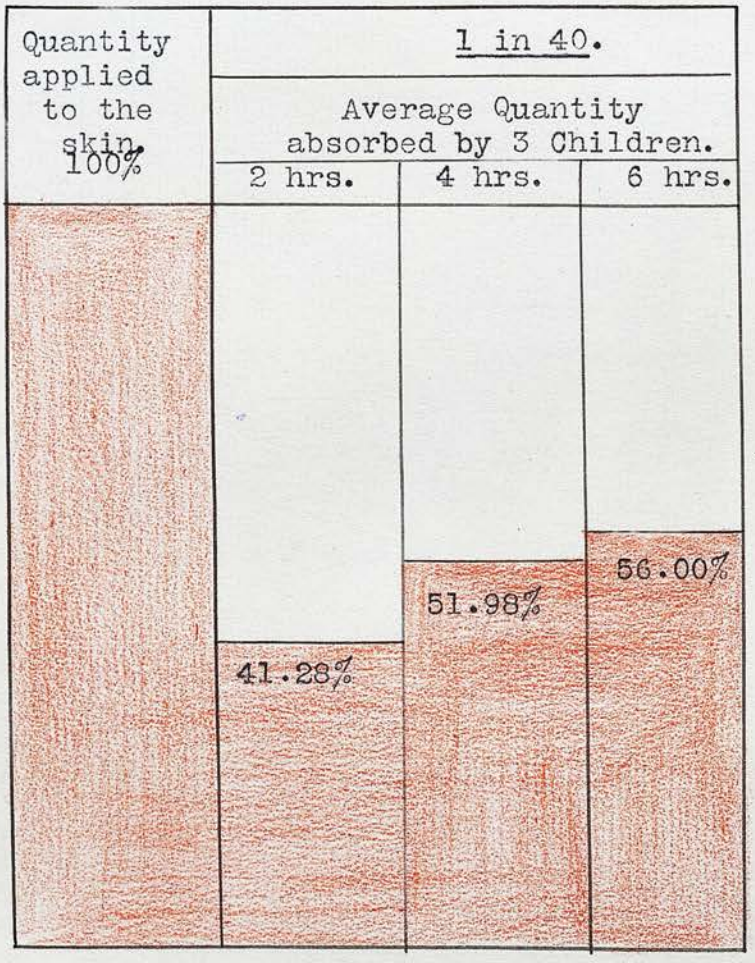
Averages of 1 in 40 over 36, 62 & 108 sq. in.

Time	per cent	per sq. in.	Total Phenol.	Ratio.
2 hrs.	41.28	7.17	537.67	1
4 hrs.	51.98	9.02	667.17	1.24
6 hrs.	56.00	9.72	742.92	1.38

The adults showed more uniformity. When the time of the application is lengthened to 4 hours the corresponding figures are 51.98 per cent or 667.17 mgrs. showing a proportion of 1.24:1 to those of the former time; i.e., only a quarter of the amount which was absorbed in the first two hours becomes absorbed during the second.

Again, there is a considerable variation among the different subjects, the percentages ranging from 36.6 per cent to 74.5 per cent, which variation corresponds more or less with that of the adults. When the duration of the application is still further increased to 6 hours there is only a very slight increase of Phenol absorbed over that of the 4 hours period, viz. from 51.98 per cent to 56.00 per cent, or from 667.17 Mgrs. to 742.92 mgrms., a ratio as compared with the two hours' period of 1.39:1, or 1/3 more is absorbed in the whole six hours as was absorbed in the first two hours.

Diagram 14.


Quantity applied to the skin.
100%
1 in 40.
Average Quantity absorbed by 3 Children.
2 hrs.
4 hrs.
6 hrs.
41.28%
51.98%
56.00%

These figures indicate that the lengthening of the time beyond two hours only slightly increases the quantity; and not only so, but that the six hours' period does not show anything like the same increase over the four hours, that this latter does over the two hours' period; for, of the 56 per cent absorbed within 6 hours, 41.28 per cent is accounted for by the first two hours, 10.6 per cent by the second two hours, and 4.02 per cent by the last two hours.

With respect to the influence of time, therefore, I find that in double the length of time about one quarter more, and in treble the length of time about one third more becomes absorbed than in the two hours. So it will be seen that of the total quantity of Phenol absorbed by a child the greatest bulk of it is effected within the first two hours. (cf. Diagram 14.)

Next, let us consider how increase of surface affects the absorption in the child. Thus taking again the 1 in 40 solution as before, I observe that when applied over 36 sq. in. 63.8 per cent or 399.08 mgrs. of it becomes excreted in the urine (cf. Table 17)

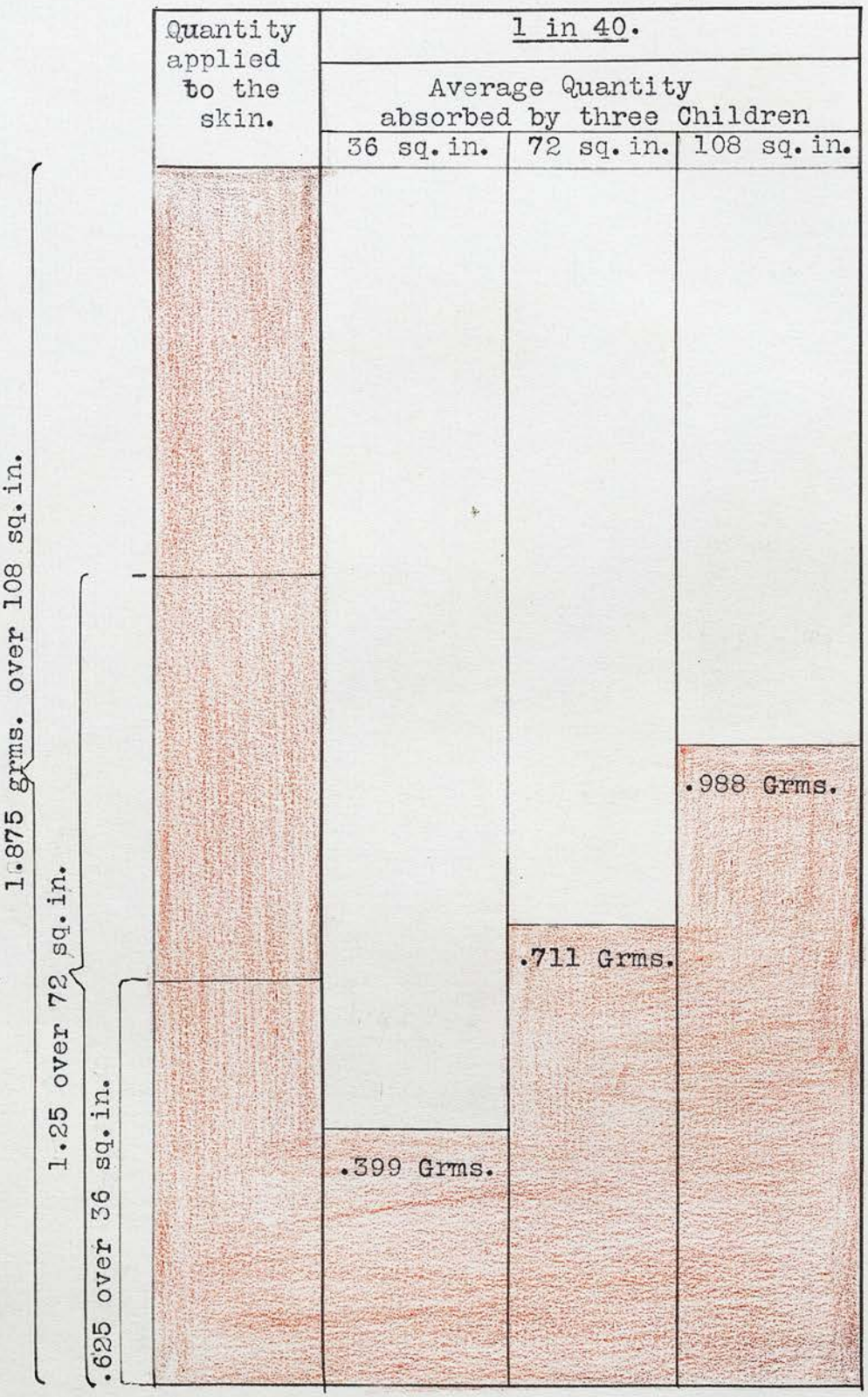
Children — Table 17

Averages of 1 in 40 for 2, 4, & 6 hours.

Surface.	per cent.	per sq. in.	Total Phenol.	Ratio.
36 sq. in.	63.8	11.07	399.08	1
72 " "	48.2	8.37	711.42	1.78
108 " "	43.14	7.49	988.59	2.48

the different individuals having absorbed fairly uniform proportions. When it is applied for the same length of time over twice this area, viz. 72 sq.in. it is seen that the percentage absorption is diminished to 48.2 per cent, but still the total quantity absorbed is increased to 711.42 mgrs. or 3/4 more than was absorbed for 36 sq.in. And when I apply the same lotion for the same length of time over three times the extent of the original surface, the percentage absorption is still more diminished, viz. from 48.2 per cent to 43.14 per cent, whereas the average total quantity of Phenol excreted is greatly increased over that for 72 sq.in., viz. from 711.42 mgrs. to 988.59 mgrs. or 1½ times more than was absorbed over 36 sq.in. So, although there is relatively to the quantity of Phenol applied to the skin a smaller proportion absorbed as the surface becomes increased to twice and three times its original size, still, there is an increased absorption of nearly ¾ and 1½ times more than was absorbed over ½ and 1/3 of the surface respectively; whereas it will be remembered that only ¼ and 1/3 of the amount that was absorbed in the first two hours became respectively absorbed in the second, and third 2 hours, probably to be accounted for by there being less Phenol

Diagram 15.


Quantity applied to the skin.
1 in 40.
Average Quantity absorbed by three Children
36 sq. in.
72 sq. in.
108 sq. in.
1.875 grms. over 108 sq. in.
1.25 over 72 sq. in.
.625 over 36 sq. in.
.399 Grms.
.711 Grms.
.988 Grms.

left in contact with the skin to be absorbed during the last four hours owing to so much having been absorbed within the first two hours, or probably owing to the balance being earlier established on the two sides of the septum. (cf. Diagram 15.)

When a weaker solution is taken, such as 1 in 80 instead of 1 in 40 and its absorption considered with respect to the influence of time and space, the ratios of increase between the different areas and periods will be seen to correspond as nearly as possible to those of the 1 in 40 solution.
(cf. Tables 18 & 19. and Diagrams 16 & 17.)

Children. Table 18

Averages of 1 in 80 over 36, 72 & 108 sq. in.

Time.	per cent.	per sq. in.	Total Phenol.	Ratio.
2 hrs.	32.72	2.84	195.61	1
4 "	45.77	3.97	255.67	1.39
6 "	48.97	4.25	294.58	1.50

Children. Table 19.

Averages of 1 in 80 for 2, 4 & 6 hours.

Surface.	per cent.	per sq. in.	Total Phenol.	Ratio.
36 sq. in.	47.68	4.13	149.02	1
72 " "	39.33	3.41	246.11	1.65
108 " "	39.38	3.41	369.74	2.48

Diagram 16.

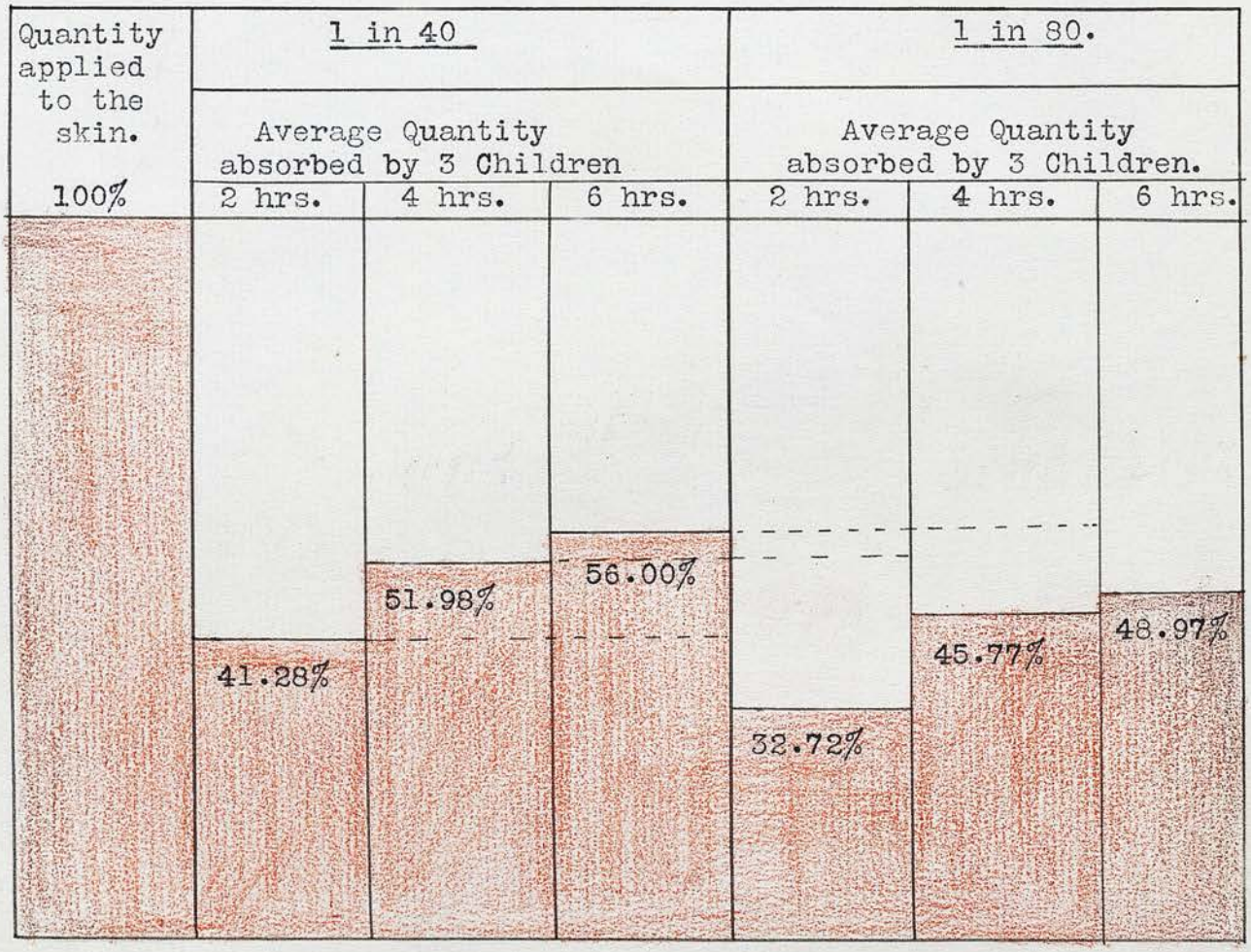
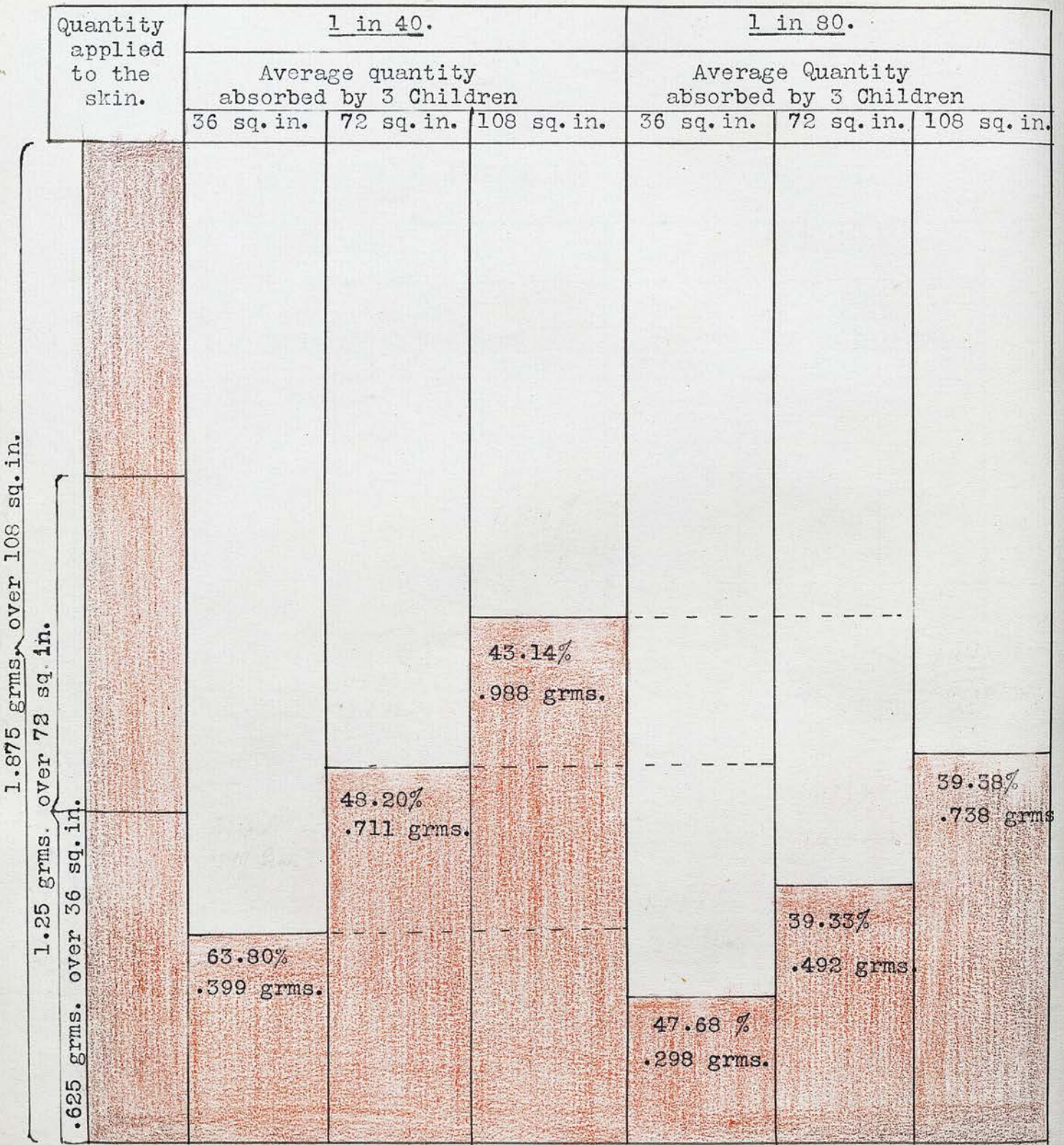

Quantity applied to the skin.
100%
1 in 40
Average Quantity absorbed by 3 Children
2 hrs.
4 hrs.
6 hrs.
1 in 80.
Average Quantity absorbed by 3 Children.
2 hrs.
4 hrs.
6 hrs.
41.28%
51.98%
56.00%
32.72%
45.77%
48.97%

Diagram 17.


Quantity applied to the skin.
1 in 40.
1 in 80.
Average quantity absorbed by 3 Children
Average Quantity absorbed by 3 Children
36 sq. in.
72 sq. in.
108 sq. in.
36 sq. in.
72 sq. in.
108 sq. in.
1.875 grms. over 108 sq. in.
1.25 grms. over 72 sq. in.
.625 grms. over 36 sq. in.
63.80%
.399 grms.
48.20%
.711 grms.
43.14%
.988 grms.
47.68 %
.298 grms.
39.33%
.492 grms.
39.38%
.738 grms

As a resume it may be stated that with delicate skins, either those of children or young females, while by increasing the extent of skin surface there is very nearly an equal proportional increase in the absorption, there is by increasing the time beyond 2 hours only a perceptible increase, almost the whole absorption taking place during the first two hours.

The question also arises whether with children also more is proportionally absorbed from a weaker than from a stronger solution. It is rather strange to find that with them the case is the reverse of what it is with the adults, the weaker solutions being then less quickly absorbed. (cf. Tables 20 & 21.) (cf. diagrams 16 & 17).

Children

Table 20

Comparison of Averages of Time.

	1 in 40			1 in 80				
Time.	per cent.	per sq. in.	Total Phenol	per cent.	per sq. in.	Phenol.	1 in 40 :	1 in 80.
2 hrs.	41.28	7.17	537.67	32.72	2.84	195.61	1 :	.79
4 "	51.98	9.02	667.17	45.77	3.97	255.67	1 :	.88
6 "	56.00	9.72	742.92	48.97	4.25	294.58	1 :	.87

Comparison of Averages of Surface. Table 21.

	1 in 40			1 in 80				
Surface.	per cent.	per sq. in.	Total Phenol.	per cent.	per sq. in.	Phenol.	1 in 40 :	1 in 80.
36 sq. in.	63.80	11.07	399.08	47.68	4.13	149.02	1 :	.75
72 " "	48.20	8.37	711.42	39.33	3.41	246.11	1 :	.81
108 " "	43.14	7.49	988.59	39.38	3.41	369.74	1 :	.91

and on the averages over all three areas and during the three periods the 1 in 40 solution shows a proportion of 1 :.86 to the 1 in 80 solution (cf. Table 22)

Children

Table 22.

Comparison of Grand Averages for 2, 4 & 6 hours over 36, 72 & 108 sq. inches.

Strength.	per cent.	per sq. in.	Total Phenol	Ratio.
1 in 40	49.22	8.54	642.27	1
1 in 80	42.30	3.67	248.20	.86

In the foregoing experiments I have dealt with changes observed by variations of time, of space and of strength of solution in adults and in children.

The next - a very important subject of enquiry - will be to ascertain the differences arising from the nature of the skin.

COMPARISON OF ADULTS WITH CHILDREN.

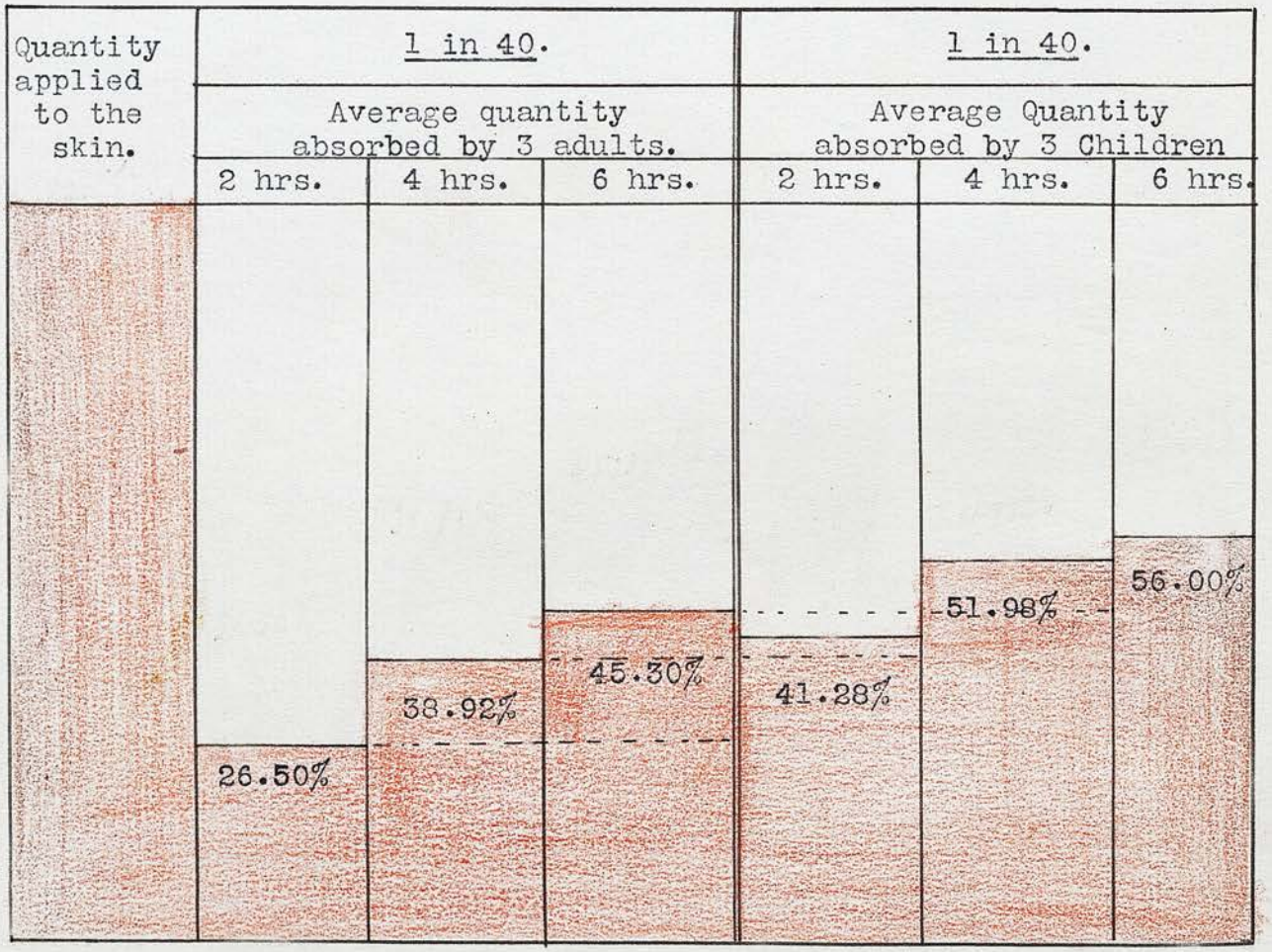
This I do by comparing the average results in the adults with those of the children with respect to time and by applying a solution of the strength of 1 in 40. By referring to Table 23 it will be noticed that while the adult absorbs during the first two hours an average total of 304.93 mgrs. the child absorbs under similar conditions an average of 537.67 mgrs. or $\frac{3}{4}$ times more than the adult, the exact ratio being 1.76 : 1. From these data we have no great difficulty in observing the great absorptive power of the more delicate skin of the child, as compared with the coarser one of the adult; and hence I am not at all astonished at the greater number of Carbolic Acid poisonings occurring in children. So these intoxications need not be attributed to any idiosyncrasy in the child; the fact solely lies in the nature of their skin and the effect of the drug upon their more vulnerable nervous system.

Table 23.

Comparison of Adult & Child.

Time.	Adult			Child			Ratio.
	per cent.	per sq. in.	Total Phenol.	per cent.	per sq. in.	Total Phenol.	Adult : Child.
2 hrs.	26.5	4.60	304.93	41.28	7.17	537.60	1 : 1.76
4 "	38.92	6.75	483.75	51.98	9.02	667.17	1 : 1.37
6 "	45.30	7.86	538.08	56.00	9.72	742.92	1 : 1.39

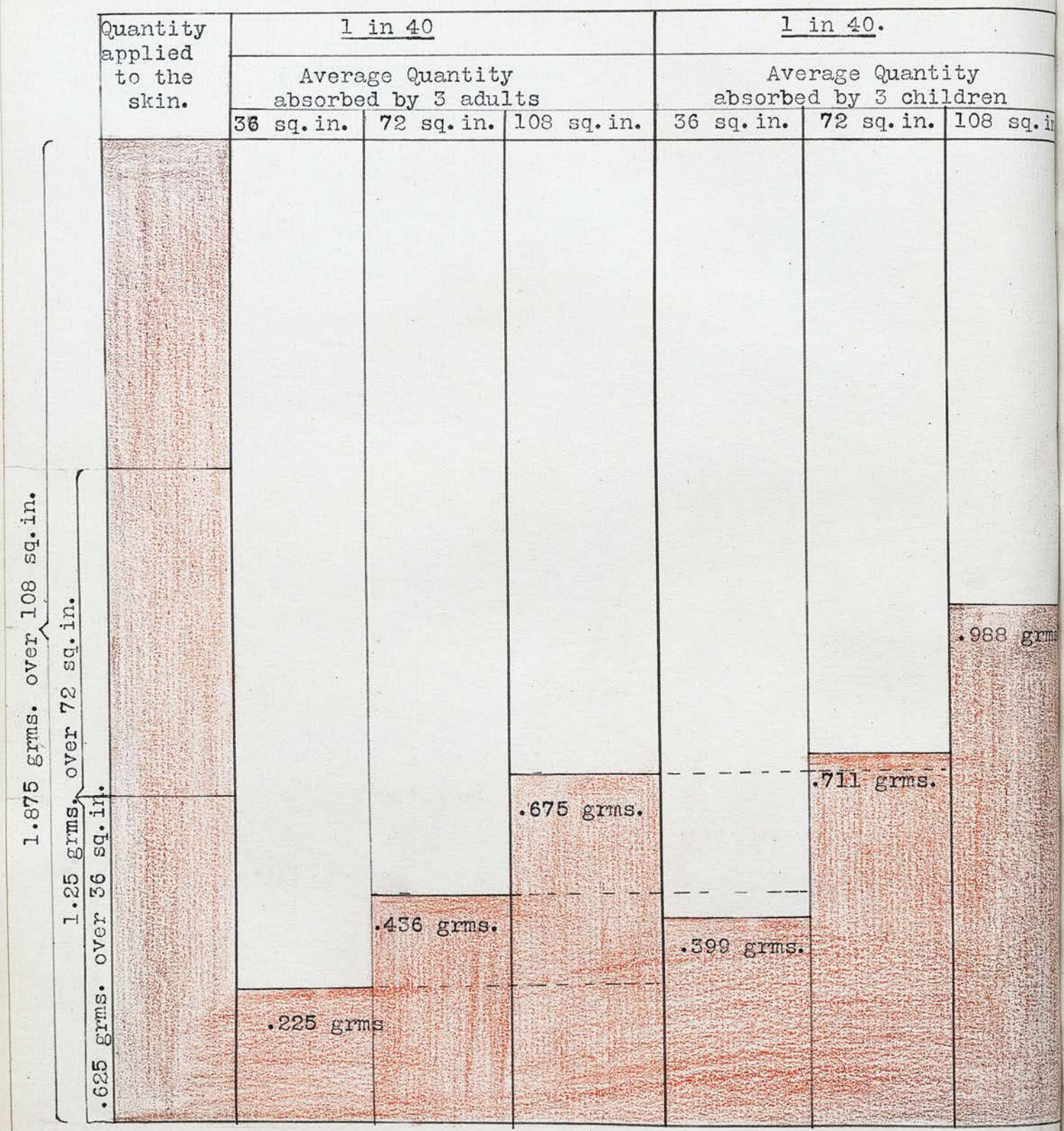
Diagram 18.


Quantity applied to the skin.
1 in 40.
Average quantity absorbed by 3 adults.
2 hrs.
4 hrs.
6 hrs.
1 in 40.
Average Quantity absorbed by 3 Children
2 hrs.
4 hrs.
6 hrs.
26.50%
38.92%
45.30%
41.28%
51.98%
56.00%

With infants whose skins are even more delicate, this will be much more the case. (cf. diagram 18.)

Were If their results be compared over the four hours' periods, there is not nearly such a marked contrast; for while the adult has a total absorption of 483.75 mgrs. the child absorbs 667.17 mgrs. or in the ratio of 1 : 1.37. This is due to the fact already observed that with children very nearly all the absorption that takes place is effected within the first two hours, only $\frac{1}{4}$ more being absorbed during the second two hours, probably because so little Phenol is left in the poultice for absorption. Whereas in adults although not so much is absorbed during the first period, there is an increase of more than $\frac{1}{3}$ during the second two hours. This is a very remarkable fact and from a surgical aspect most important in the external application of Phenol. Finally, it is noticed that while the adult absorbs 538.08 mgrs. in 6 hours' time, the child absorbs under similar conditions 667.17 mgrs. in the corresponding time, or in the ratio of 1.39 : 1, as compared with the adult. So it is seen that the greatest difference between the child and the adult is in the absorption during the first two hours $\frac{3}{4}$ more being absorbed by the child; and also, that while the child absorbs hardly anything during

Diagram 19.


Quantity applied to the skin.
1 in 40
Average Quantity absorbed by 3 adults
36 sq. in.
72 sq. in.
108 sq. in.
1 in 40.
Average Quantity absorbed by 3 children
36 sq. in.
72 sq. in.
108 sq. in.
1.875 grms. over 108 sq. in.
1.25 grms. over 72 sq. in.
.625 grms. over 36 sq. in.
.225 grms
.436 grms.
.675 grms.
.399 grms.
.711 grms.
.988 grms

the second and third periods, the adult goes on absorbing considerable quantities; and so, the longer the poultices are allowed to remain on the skin in both cases, the more nearly will the quantities absorbed by the child and adult approach one another. And hence, there can be no doubt that the absorption in children is far more rapid than in adults.

The effect of varying the space covered shows hardly any appreciable difference between the adult and child since over 72 and 108 sq.in. both absorb about $\frac{3}{4}$ and $1\frac{1}{2}$ times more than is absorbed over 36 sq.in.; that is, the ratios of the amounts absorbed stand in both cases to the ratios of the different surfaces in a similar relation. (cf. diagram 19.)

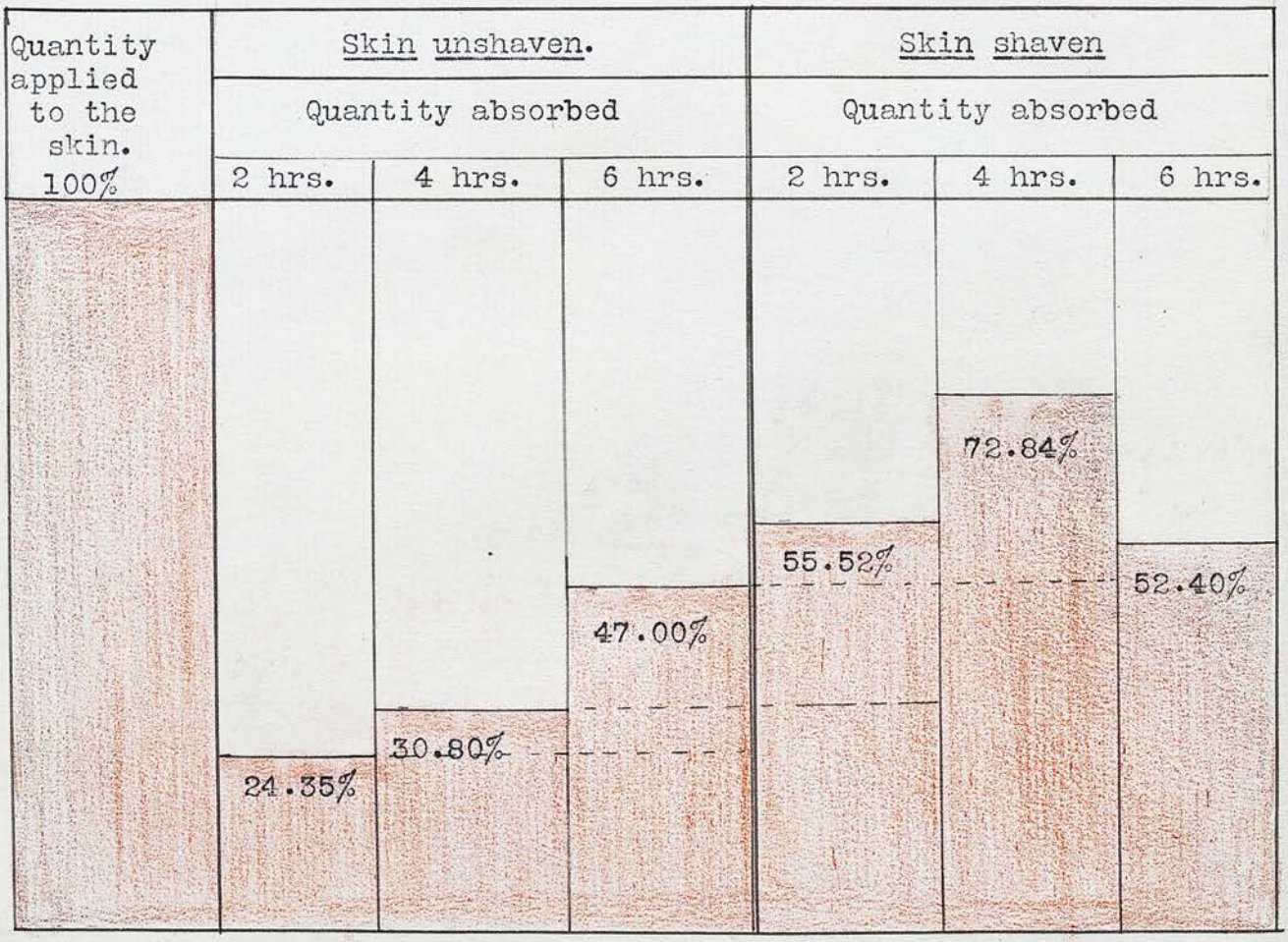
This will become much clearer by a reference to Table 24. As observed before I repeat that the child absorbs more from a 1 in 40 solution relatively to the quantity applied than from 1 in 80 solution, while the adult absorbs more from the 1 in 80 than from the 1 in 40; but the differences are so slight that they are scarcely worth consideration.

Table 24.

Comparison of Adult & Child.

Surface.	Adult				Child.			
	per cent.	per sq. in.	Total Phenol	Ratio	per cent.	per sq. in.	Total Phenol.	Ratio
36 sq. in.	40.92	7.10	255.90	1	63.8	11.07	399.08	1
72 " "	34.88	6.06	436.62	1.70	48.2	8.37	711.42	1.78
108 " "	35.97	6.25	675.41	2.64	43.14	7.49	988.59	2.48

Diagram 20.


Quantity applied to the skin.
100%
Skin unshaven.
Quantity absorbed
2 hrs.
4 hrs.
6 hrs.
Skin shaven
Quantity absorbed
2 hrs.
4 hrs.
6 hrs.
24.35%
30.80%
47.00%
55.52%
72.84%
52.40%

COMPARISON OF SHAVEN & UNSHAVEN SKIN.

Up to this point the experiments have all been made with the skin merely washed with soap and hot water. The question now arises for solution whether by thoroughly preparing the skin by means of shaving, scrubbing with soap and hot water, then washing with ether, etc., as is done ordinarily in hospital practice, there will be any difference in its absorptive powers. I therefore carried out a series of experiments with subject A, whose skin was thus"prepared", and shall now compare the results with those of his unprepared skin, all other conditions having been the same. Thus, by a reference to Table 25, it is seen that the"prepared"skin absorbs in 2 hours more than double the amount absorbed by the unprepared in the same time, the ratio being 2.28 : 1. In 4 hours' application a more or less similar result is observed, the ratio being 2.36 : 1. When, however, I compare them over a period of 6 hours the ratio is very much lessened, being now 1.114 : 1, or only 1/9 more is absorbed by the "prepared" than by the unprepared. (cf. diagram 20, Tables 25 & 30).

Table 25.

Comparison of Shaven & Unshaven Skins.

Time.	Skin unshaven			Skin shaven & "prepared"			Ratio		
	per. cent.	per sq. in.	Total Phenol	per cent.	per sq. in.	Total Phenol.	Unshaven skin	:	Shaved skin
2 hrs.	24.35	4.23	216.43	55.52	9.64	713.24	1	:	2.28
4 "	30.80	5.35	390.62	72.84	12.65	870.30	1	:	2.36
6 "	47.00	8.16	548.05	52.40	9.09	682.33	1	:	1.114

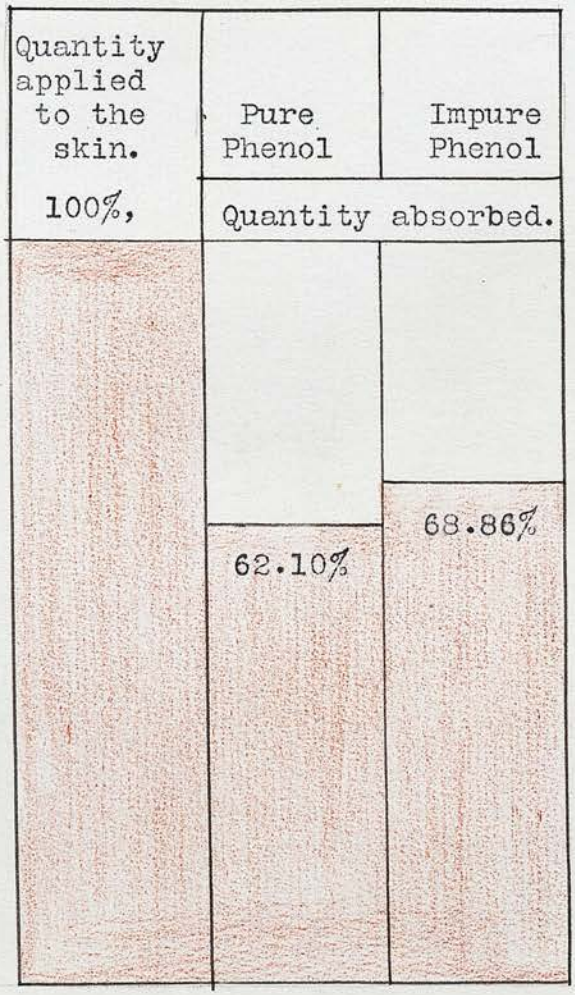
The probable reason for this decrease is the fact that during the first 4 hours most of the Phenol had been absorbed, leaving but little in the poultice for the 5th and 6th hours, whereas with the unprepared skin, the action being weaker, and consequently not so much having been taken up during the earlier hours, a greater quantity remains in contact with the skin during the last 2 hours.

All through, this seems to indicate to me that the quantity absorbed depends greatly on the amount of phenol remaining in contact with the skin.

So by supersaturating a compress we can well understand that length of time will influence greatly the total amount absorbed. The effects of thus "preparing" the skin is, not only to greatly increase the vascularity of the part, rendering it almost hyperaemic at the time the application is made; but it also opens up the ducts of the sebaceous and sudorific glands, and hence their increased action causing a greater absorption.

Langenbuch (L.C.) long ago in his clinics found that by opening up the pores as by shaving or stretching the skin (cf. case quoted in the Literature) an increased amount was absorbed, so much, indeed, as to give rise to Carbolic Acid intoxication. (Berlin.Klin. Wochensch. Bd. 28, 1878, S.412.

Diagram 21


Quantity applied to the skin.
100%,
Pure Phenol
Impure Phenol
Quantity absorbed.
62.10%
68.86%

PURE & IMPURE CARBOLIC ACID .

Since there is such a diversity of opinion as to the impurities in the Phenol affecting its rate of absorption, it occurred to me that it would be of interest to ascertain the actual behaviour of the two. To this end I undertook another series of experiments with subject A with Calvert's No.4 Carbolic Acid upon a "prepared" skin surface and compared the results obtained with those with pure Phenol having a melting point of 40.9°F.

So far as my experiments went I was not able to detect any great difference between the two, but that, on the whole, the impure seemed to be absorbed slightly more rapidly than the pure in the proportion of 1.108 : 1. I also noticed that with the impure there was more local burning pain over the area covered with the poultice than with the pure phenol, which might tend to produce a certain amount of shock in children (cf. Tables 26 & 30, also diag.21)

Table 26.

Comparison of Pure & Impure Phenol.

Pure			Impure			Ratio.	
per cent.	per sq. in.	Total. Phenol.	per cent.	per sq. in.	Total Phenol	Pure	: Impure
62.10	10.79	662.79	68.86	11.96	685.60	1	: 1.108

Averages for 4 experiments

TABLE 27 (a).

1 in 40 Solution for 2 hours.

	25 cc. over 36 sq. in.			50 cc. over 72 sq. in.			75 cc. over 108 sq. in.		
	per cent.	per sq. in.	Total Phenol.	per cent.	per sq. in.	Total Phenol.	per cent.	per sq. in. (a)	Total. Phenol
A.	28.3	4.91	176.98	20.4	3.55	255.88	9.8	1.71	185.27
B.	29.3	5.09	183.36	23.8	4.13	297.72	23.5	4.08	441.51
C.	29.3	5.09	183.52	28.2	4.89	352.74	29.2	5.07	547.76
DK.	55.8	9.70	349.34	48.1	8.36	602.25	51.9	8.99	971.38
E.	(b)			27.6	4.79	345.49	24.2	4.20	454.16
D.	(c)			40.2	6.99	503.41	(c)		
	For 4 hours.								
A.	29.9	5.19	187.02	30.2	5.25	378.13	32.3	5.61	606.68
B.	41.9	7.27	261.89	31.4	5.45	392.66	40.5	7.03	760.11
C.	50.9	8.83	318.18	48.1	8.36	602.47	45.1	7.83	846.61
DK.	74.5	12.90	465.81	56.7	9.83	708.16	51.3	8.92	963.55
E.	(b)			40.8	7.09	510.94	36.6	6.36	687.37
D.	(c)								
	For 6 hours.								
A.	63.8	11.10	398.92	32.6	5.67	408.60	44.6	7.74	836.59
B.	35.5	6.16	221.97	49.5	8.60	619.77	29.3	5.09	549.71
C.	59.4	10.31	371.37	49.7	8.63	621.58	51.7	8.99	970.99
DK.	61.1	10.61	382.08	65.9	11.44	823.86	54.9	9.54	1030.85
E.	(b)			58.1	10.10	727.37	40.0	6.94	750.42
D.	(c)								

(a) Patient had influenza and perspired profusely.
(b) Child left hospital.
(c) Child took scarlatina.

TABLE 27 (b).

1 in 80 Solution for 2 hours.

	25 cc. over 36 sq. in.			50 cc. over 72 sq. in.			75 cc. over 108 sq. in.		
	per cent.	per sq. in.	Total Phenol.	per cent.	per sq. in.	Total Phenol.	per cent.	per sq. in.	Total Phenol.
A.	12.6	1.09	39.44	26.3	2.28	164.52	17.2	1.49	161.71
B.	32.1	2.78	100.23	18.6	1.61	116.56	34.4	2.99	323.18
C.	31.2	2.71	97.49	27.5	2.39	172.45	27.8	2.41	261.31
DK.	56.4	4.89	176.11	41.0	3.56	256.33	32.6	2.83	306.28
D.	19.2	1.66	59.85	21.7	1.88	135.67	25.5	2.21	239.42
				For 4 hours					
A.	45.1	3.91	141.08	34.7	3.01	217.35	27.3	2.37	256.08
B.	16.2	1.40	50.74	63.4	5.51	396.85	40.1	3.48	376.07
C.	62.8	5.45	196.27	67.5	5.86	422.17	55.8	4.85	523.96
DK.	67.7	5.87	211.63	46.1	4.00	288.53	47.9	4.16	449.90
E.	29.4	2.54	91.76	37.8	3.28	236.56	(a)		
				For 6 hours.					
A.	37.3	3.24	116.66	60.9	5.29	381.03	21.7	1.88	204.02
B.	55.6	4.82	173.68	31.5	2.73	197.12	49.0	4.25	459.80
C.	69.4	6.02	216.84	58.0	5.04	362.87	42.8	3.72	401.97
DK.	51.7	4.49	161.68	44.3	3.85	277.26	57.5	4.99	539.96
E.	61.8	5.36	193.11	45.1	3.92	282.32	33.4	2.89	313.15

(a) Urine not properly collected owing to a misunderstanding.

INDIVIDUALITY.

It must already have been noticed in the course of this enquiry that great variations are found, as to the amount absorbed by different individuals, with whom the experiments were conducted under conditions precisely similar. To bring this point more into prominence I have drawn up a Table (No. 27) which illustrates this part of our discussion very well, and to which I shall advert in the remarks I have to make.

While I give a certain number, as denoting the average absorption during a certain period, when I come to examine the various items from which the average was derived, I find that these differ widely among themselves. Thus, while the average total absorption during a period of 4 hours with 25 cc. of a 1 in 40 solution applied over 36 sq.in. is 255.69 mgrs; the extremes under these conditions are 187.02 mgrs for A, and 318.18 mgrs. for C, the one having nearly the double of the other.

Again, the average for adults during a 4 hours' period with 75 cc. of a 1 in 40 solution applied over 108 sq.in. is 737.8 mgrs., the absorption for subject A. being 606.68 mgrs. while C. has 846.61 or about

1/3 more. These differences in the absorption of individuals are even more noticeable among the children. While the average total for them is 426.56 mgrs. with 75 cc. of a 1 in 80 solution applied over 108 sq.in. for a period of 6 hours, the quantities excreted by DK. and E. are respectively 539.96 mgrs. and 313.16 mgrs., showing a difference of 226.8 mgrs. Again, we have an average of 483.72 mgrs. for children with 50 cc. of a 1 in 40 solution applied over 72 sq.in. for 2 hours and the variations in the individuals ranging from 345.49 mgrs. to 602.25 mgrs., the latter approaching the double of the former. One might say that this resulted from the different natures of the different skins. In the adults experimented with, however, the only distinction observable in the nature of the skin was that that of A. was rather of coarser texture than that of C; and with the children, DK's skin was perhaps the more delicate of the two.(a) These facts as stated, definitely show that some persons have a decidedly greater absorptive power than others; and it throws light on the circumstance that external applications of Carbolic Acid which are quite safe to some, are productive of grave consequences to others.

(a) Although DK is older than E by $2\frac{3}{4}$ years.

What is therefore known as "Carbolic Idiosyncrasy" so far as that is concerned with external applications, is resolvable very much into an excessive absorptive power of the skin.

But not only do different individuals vary in absorptive power, but the same person, when experimented with at different times, is found to excrete different quantities of Phenol, although the conditions may be exactly the same. For example, on one occasion C. excreted over a surface of 72 sq. in:, from a 1 in 80 solution, 422.17 mgrs. during 4 hours, while at another time 362.87 mgrs. in 6 hours; thus shewing a less amount in six hours at the one time than in four at the other. Also, subject B. with the same solution applied for the same time excreted 396.85 mgrs. when applied over 72 sq. in. on one occasion, and 376.07 mgrs. when the application was over 108 sq. in. on another; that is, considerably more was absorbed from a less area at one time than from a greater area at the other. Many other instances of the same nature could be given.

During the time when the carbolic spray was in vogue, the deaths of several surgeons were attributed to Carbolic Marasmus giving rise to kidney disease. It will thus be of importance to ascertain

the Surgeon's position in this respect under the present system. To this end two surgeons who were employing Carbolic Acid as their antiseptic in operations were good enough to allow me to experiment with their urine collected after operations. In the case of surgeon G. who was engaged in operations for „Carcinoma of Stomach", "Retro-pharyngeal abscess", "Tubercular glands of the neck", for 2½ hours, and who had previously as well as during the intervals purified his hands with Lysol and a 1 in 40 Carbolic lotion; and who, during the operations employed for the most part a 1 in 40 solution, as well as a weak Boracic acid lotion, excreted within 26½ hours following, 90.26 mgrs. of Phenol over and above his normal excretion of 128.36 mgrs. On another occasion, when engaged in operations for "Abscess of the Liver", "Ischio-rectal abscess", "Tumour behind Oesophagus" and "Cold abscess of the Knee", he excreted 226.26 mgrs. beyond his normal quantity, having prepared himself exactly in the same manner as before (cf. Experiments 131 & 132).

Surgeon H. was engaged in operations for 3½ hours, having 5 different operations in that time, viz., for "Two cases of glands in the neck", "Mastoid Disease",

"Abscess about the groin" and " a cleft palate." His hands were washed chiefly with Lysol, but subsequemtly he used a little of a 1 in 20 Carbolic lotion and plenty of 1 in 60. His excretion, over above his normal rate, was 322.47 mgrs. in the following 24 hrs. At another time, under similar conditions as regards Carbolic Acid, while engaged for 2½ hours in three operations,viz. "Glands in the neck, "Excision of the Hip Joint," and "Double knock-knee." he excreted 355.35 mgrs. in 28 hours from the time of operation. These quantities correspond more or less with what is absorbed when a 1 in 40 poultice is applied over 72 sq. in. during 4 hours. It is therefore seen that the most phenol is absorbed when the surgeon deals with operations where the hands require to be often dipped in the solution, either from the nature of the operation demanding it, or from the number of operations.

Amounts such as these passing daily through the system, and particularly through the kidneys must have a great tendency to set up irritation in these organs; and thus one is not at all surprised at the Carbolic Marasmus of Czerny which used to be so often manifested in operating surgeons employing the spray.

In the course of my experiments the only signs

of injurious action observed in the subjects were, Carboluria in several instances as will be seen by referring to Table 28)., and in experiment 126 the subject complained of considerable restlessness during the night of the application; otherwise they were all quite well. Large quantities of Carbolic Acid may pass through the system without giving rise to any sign of poisoning. In one case, experiment 127, as much as 1.332 grammes were excreted by an adult in 24 hours, without him having complained of any uneasiness. Falkson (Arch. für Chir, Bd. 26, 1881, S.204) gives an instance where about 4 grammes were absorbed by a patient treated by the Listerian method; but in this case toxic effects, which soon passed away again, were produced.

One of my subjects had an attack of Influenza when under experiment; he perspired very freely during the night and the most part of the Phenol must have been thrown out of the system by this channel, for very little more than the normal quantity was found in the urine (Experiment 59).

This suggests that in the treatment for Carbolic Acid poisoning, free sweating might be resorted to with good effect, and also that surgeons should keep their skins in good order.

According to Falkson, the most characteristic proof of Carbolic Acid intoxication is certainly Carboluria. This term is applied to the brown or green colouration produced in the urine by the presence of an excess of Phenol derivatives, viz. Hydrochinon, Pyrocatechin and other oxydation products. Sometimes even, it is the only pathognomic symptom observed, the other signs of intoxication being wanting, and hence it is of great importance to know its toxic significance. No doubt the significance of it has been overestimated by some and too much disregarded by others, such as Salkowski, Kuester, Nothnagel, Kossbach, Hoppe-Seyler and others. To Falkson (Arch. f. Klin Chir. Bd. 26, 1881, S.217) who made a series of careful observations in patients affected with Carboluria, that resulted from treatment by the Listerian method, we are indebted for its real value. This writer showed that the colour of the urine varies in depth with the proportion of Phenol contained in it, the greater the proportion of the Phenol is, the more intense being the colouration. Because urine, which contains only small quantities or mere traces of Phenol, never takes on the black brown or green colour which he had observed, when larger quantities of it were present.

The same conclusion is indicated by the fact, that, when fresh additions of Carbolic Acid are excluded from the system, the colour gradually fades and eventually returns to normal. Also, that the intensity of the colour is proportional to the quantity of Phenol in the system is quite in keeping with the fact, that the dark colouration is produced by Hydrochinon, Pyrocatechin and similar substances, (Baumann & Preusse, Zeitsch. f. Phys. Chem. Bd.3, S.156), which are derivatives of Phenol. These must hence be developed in greater quantities, the more Phenol is absorbed and becomes excreted. The colour, too, varies with the percentage proportion, since, when this is lowered by the addition of water, the intensity of the colour is also diminished; whereas, when the urine is concentrated, as by evaporation, the colour becomes more marked. My observations accord with those of Falkson, for I noticed during evaporation, that colours which were only slight before, became more marked during the process, and that, as a greater quantity of Phenol becomes excreted in the same person, so the colour is more pronounced and vice versa, (cf. Experiments 16,20 & 24 DK,45 & 51C,63,67 & 73 A. Table28). Very nearly all the instances in which Carboluria was observed were those which occurred in Children. I noticed that they developed carboluria with

smaller quantities of Phenol than adults did. For, although one of the adults (cf. Experiment 127A) excreted far larger quantities of Phenol, he never developed Carboluria; while on the other hand, nearly all the children excreted smaller quantities and showed colouration of the urine. The probable reason for this is that the quantity of urine in the child is much less than in the adult, and so there is present a more concentrated solution of Phenol in the former case. Taken by itself, the colour of the urine is not altogether to be depended on as a sign of danger, but should be considered along with the Reaction, the Specific Gravity, and the quantity passed daily. Like Falkson, I always found the urine acid. The specific gravity I did not take however, but according to the same writer this stands in direct relation to the percentage composition of the urine with respect to Phenol derivatives, and to the intensity of the colour, i.e. the more marked these are, the higher is the specific gravity. He also observed that, as a rule, when the system is under the influence of Phenol, the total quantity of urine becomes diminished, and this diminution stands in direct relation to the quantity of Carbolic Acid administered; for in a patient in whom he daily increased the quantity of

Phenol the total quantity of urine likewise became diminished. In my experiments, however, this did not appear to me to be the case, at all events not with the quantities of Phenol with which I was dealing.

It might be thought that a more exact method of ascertaining the degree of intoxication would be by actual measurement of the amount of Phenol present in the urine. This estimation, however, would require time, and besides, one would require to have the urine of 24 hours and serious consequences might follow before the estimate was completed. There is need, therefore, of some more speedy and ready way of ascertaining whether the Phenol is present in such quantities as to threaten danger. To this end in my experiments, in addition to estimating the quantity of phenol, I also employed a modification of Sonnenburg's (Deutsche Zeitsch. f. Chir. Bd. 9, 1878, S.356) method of estimating the Sulphates found in the urine, in a way that, I thought, might be readily used in ordinary practice. A quantity of urine, previously acidulated with Acetic Acid and boiled, is measured with a minim measure and its Sulphates precipitated with Barium Chloride. From previous statements, it will be understood that, commonly, the greater the

amount of Sulphates present, the less is the Phenol, since the latter takes up these to form Phenol-Sulphuric acid salts. I did not however find this estimate of much use; for in cases where there were considerable quantities of Phenol, I noticed that the Sulphates were also increased, I suppose, probably due to change of diet. Besides, here again, one would require to know the normal amount of Sulphates present in a measured quantity of urine in any individual case, in order to draw a comparison with it. And, as pointed out by Falkson (L.C.) one might get scarcely any precipitate of Sulphates and yet not be dealing with an intoxication. So by itself the presence or absence of Sulphates is not of very great value, but should always be considered along with the colour, reaction, specific gravity and daily quantity of the urine. So one must not lose sight of the fact, that it is not always necessary immediately to discontinue the use of Carbolic Acid, probably to the detriment of the patient, when Carboluria sets in; but much better is it to direct one's self, in such cases, along with it to the intoxication symptoms of which disturbances of the digestive & the nervous systems, e.g. nausea, vomiting, slight headaches and ringing in the ears, are without doubt, the earliest and most important.

Taking a general review of the results of my experiments therefore, I may sum up as follows:-

1. The average absorption or excretion of an adult from the external application of a solution of 1 in 40 Carbolic Acid is 26.5 per cent, of what is applied to the skin for the first 2 hours; 38.92 per cent for 4 hours or ½ more than for 2 hours; 45.30 per cent for 6 hours or ¾ more is absorbed in 6 hours than was absorbed in 2 hours. Although these are the averages for 3 adults, the result of the individual subjects almost exactly corresponded.

2. By using a weaker solution, e.g. 1 in 80, in adults, while there is actually a less amount absorbed, yet, relatively to the quantity applied, a greater percentage enters the system in the ratio of 1:1.06; in other words, by diminishing the surface and increasing the strength of solution less becomes absorbed than over the larger surface. In children relatively more of the 1 in 40 than of the 1 in 80 becomes absorbed, viz. in the ratio of 1:.86.

2a. In adults and children as the surface for absorption is increased to twice its former size, viz.72 sq. in, so also ¾ more is absorbed than over 36 sq.in. and as it is increased to 3 times its size, viz.108 sq.in. so 1½ more becomes absorbed than was absorbed over 36 sq.in.

So the results in children and adults are more marked by increasing the skin surface covered than by increasing the duration of the application.

3. By having the skin shaved and "prepared" in the way usually practised in Hospitals, prior to operations, I noticed that within periods of 2 and 4 hours more than double the amount of Phenol respectively becomes absorbed, than is the case when the skin is not so prepared. This no doubt is due not only to the skin area being rendered more vascular, but also to the opening up of the ducts of the sebaceous and sudorific glands. In periods of time beyond 4 hours the proportion is greatly diminished, probably because, in the case of the "prepared" skin, most of the Phenol had been absorbed during the first 4 hours and so very little was left in contact with the skin during the last 2 hours.

4. By using an impure Phenol there is slightly more absorbed than with the pure, but the local irritation is much more marked.

5. Children absorb about 75 per cent or $\frac{3}{4}$ times more than adults do during the first 2 hours; but as the periods of time are extended, this ratio diminishes to about 1.38 from 1.76, i.e. that during 4 and 6

hours children absorb only about 2/5 more than adults.

6. Of the total quantity of Phenol absorbed by a child in 6 hours, the greatest bulk of it, viz. 41.28 per cent, takes place during the first 2 hours only ¼ and 1/3 more being absorbed in 4 and 6 hours respectively. On the other hand, while there is less absorbed by an adult during the first 2 hours, there is still a considerable increase during the 2nd and 3rd periods, ½ and ¾ more being respectively absorbed. This is a point of great importance in practice, and probably accounts for the numerous cases of Carbolic Acid intoxication among children in whom the absorption is very rapid indeed. A considerable amount of Phenol entering the system gradually, and over a more lengthened period of time, might not produce any serious effect upon the nervous system directly, since while it is being absorbed, time is also allowed for it to become excreted and thus no large quantity can be present in the system at one time; and therefore, although it may have injurious effects on some particular organ, such as the kidney, by its continual action during excretion, toxic effects are not likely to be produced. Whereas in children, with whom the absorption is very rapid, there is a large amount of Phenol entering the system at once and

so not sufficient time is allowed for it to be thrown out again. As this will allow a large quantity to be present in the system at one time, it may act as an over-dose of the drug and give rise to toxic effects by its action on the very vulnerable central nervous syetem of children. With infants whose skins are even more delicate, this danger is greatly increased.

7. Different individuals show wide differences in absorptive action, even when circumstances are exactly similar, in all probability due to the different nature of their skins.

8. The same person absorbs in different degrees at different times.

9. Operating surgeons on an average absorb about 248.57 mgrs. during 2½ or 3 hours' operation, or about as much as is done by an adult in 4 hours when 50 c.c. of 1 in 40 solution are applies over 72 sq. ins.

10. Children show carboluria sooner and with smaller quantities of Phenol than adults.

Practical Applications of the results of my investigations.

It has been conclusively shown that delicate skins such as those of infants, children, and young females have very great absorptive energy, and that with them the Phenol very rapidly enters the system. We saw that practically all that became absorbed entered the system in the first 2 hours; so, if no toxic symptoms manifest themselves at the end of this period, the poultice could be left on with safety for a longer time, if necessary.

Since serious results, such as the paralysis of the Heart or Lungs, arising from the action of the drug up the nerve centres, depend upon the presence of a large quantity of the substance in the system at one time, rather than the amount passing through the body during a more or less lengthened period, it is plain that is must be dangerous to apply Carbolic poultices over large areas in such cases. The danger is not averted, as some might think, by taking weak solutions over large areas instead of stronger ones over a limited space; for it was seen that with adults at any rate, dilute solutions were relatively more rapidly absorbed than strong. It will be remembered that the

experiments showed that absorption varies in almost a direct ratio with the extent of surface covered.

In the case of infants, although I did not experiment with them, it is not making any unwarranted assumption to say that in their case the great delicacy of skin must make it peculiarly unsafe to use Carbolic Acid as a disinfectant. With children, and particularly with infants, its employment for the purpose of purifying the skin previous to operation had therefore better be altogether avoided. If it should be found necessary that their skin should be purified, a Boracic Acid poultice might be substituted, and at the operation more thorough means employed.

There is no doubt that the scrubbing and shaving of the skin have the effect of greatly increasing the absorption; it therefore becomes a question whether, with children and young females these should be practised. I consider that in the above mentioned cases, owing to the nature of the skin, it is hardly necessary to have recourse to shaving or scrubbing. It would be preferable to employ a Boracic Acid poultice some time previous to the operation and then at the operation more thorough means could be used for the purification. Our object is not to facilitate absorption but merely to purify the skin surface.

Therefore even in adults, when one is dealing with large areas, as in Scirrhus of the Breast, where the axilla and side of the Thorax as well as the Mamma have to be disinfected, it is doubtful whether, previous to applying the carbolic poultice, the parts should be scrubbed or shaven. Perhaps it would be a safer procedure merely to wash the parts with soap and hot water previous to applying the Carbolic poultice, and then defer the scrubbing and shaving till the time of the operation.

In operations in the neighbourhood of the Genitals however, it certainly would be advisable to shave and scrub the parts as well as apply the Carbolic poultice about 24 hours previously.

So far as my investigations went, I merely concerned myself with absorption; but it certainly would be very interesting to ascertain what difference in the germicidal value of the Carbolic Acid was occasioned by applying the poultice to a "prepared" or an "unprepared" skin.

For the sake of those who may wish to pursue this investigation further, I have constructed a "Distillate Table' (No. 29.), by reference to which an idea of the quantities of sodium Hydrate and Iodine, required to precipitate the Phenol, might be obtained.

Before concluding I wish to express my grateful acknowledgements to my esteemed chief, Prof. Fraser, for his kindness in allowing me the free use of his laboratories; to Mr. Stiles for his goodness in giving me access to his wards in the Royal Hospital for Sick Children, as well as to my friends who have assisted me in carrying out my investigations.

Materia Medica Department,

Edinburgh University,

29th April, 1899.

BIBLIOGRAPHY.

1834-1869.

1. F. F. Runge, Ann. d. Phys. und Chem. Bd. 31, 1834 s.65; and Bd. 32, s. 304.

2. Stadeler, Das regelmassigen vorkommen von phenolartiger Substanzen im Harn. Ann. d. Chem un Pharmac. Bd. 77, 1851 s.17.

3. Bulikinsky, Ueber die Carbolsaure im Harn, Hoppe-Seyler's Med. Chem Untersuchungen, Heft 2, 1867 s. 234-40.

4. Lister, J., On the Antiseptic System of Treatment in Surgery, B.M.J. Vol. 2, 1867, p. 246; Lancet Vol. 2,1867 pp. 353 & 668; B.M.J. Vol.2, 1868, p.53, 101, 461, 515.

5. Machin, Fatal cases of poisoning by the absorption of Carbolic Acid, B.M.J. Vol. 1, 1868, p. 220.

6. Almen, Urines Forandring Vid Utvartes Bruk af Carbolsyra, Upsala Lakaref Forh. V. 1869-70, pp. 253-56; also J.W.Moore, M. Press and Circ. X. 1870, pp. 305.

7. Lightfoot, Poisoning by Local Application of Carbolic Acid. B.M.J. Vol. II, 1870, pp. 331.

8. Wallace, Carbolic Poisoning by Absorption from the Skin. B.M.J. Vol. I. 1870, p. 432.

9. Huseman, Toxicologische Studien ueber Carbolsaure und Kreosot. Deutsche Klink 1871, s.350.

10. New York Med. Gazeete, Apr. 1871.

11. Landolt, Nachweis von Phenol im Harn. Berlin Chem. Berichte. Bd. 4, 1871, p.772.

Bibliography.

12. Kohler, Todliche vergiftung durch Carbolsaure als mittel gegen kratze. Wurtemburg Med. Correspon. Blatt XLII. 1872, s. 41 & 49. also Schmidt's Johr-buch, Bd. CLV. s.276.

13. Salkowski, Ueber die Wurking und das Chemissch verhalten des Carbols im Tierkorper. Pflugers Arch. V. 1872, s. 335 & 351.

14. Hoppeseyler Ueber das vorkommen des Phenol im Tierkorper, Pfluger's Arch. Bd. V. 1872 s. 470-480 saure s. 426 & 176.

15. Hamilton, Carbolic Acid as a Cerebro-spinal poison. B.M.J. I. 1873, pp. 226.

16. Salkowski, Ueber die entstchung des Phenols im Tierkorper Berl. d. Deutsch. Chem. Gesel. X. s. 842, IX s. 1595.

17. Hueter Deutscge Zeitsch fur Chir. Bd. 12 s.497.

18. V. Meiring, Die Axydation des Phenols zur Brenzkatechin und Hydrochinon. Pfluger's Arch. Bd. 14, 1876, s. 276.

19. Salkowski, Ueber das vorkommen Phenol-Vildender Substanz im Harn Bei Ileus. Centralblatt f. die Med. Wissenschaften 1876, s. 818.

20. Kopperschaar, Maas analytische Bestimmung des Phenols, Zeitsch fur Analyt. Chemie. Bd.15 s.233, 1876.

21. E. Baumann, Ueber den Ort der Bilding der Phenolschwefelsauren im Tierkorper Pflugers Arch., Bd. 13, 1876, s. 285.

22. E. Baumann, Ueber gepaarte schwefelsauren im harn, Pflugers Arch., bd. 12, 1876, s.69, Swoie Bd. 13, 1876, s. 285.

23. E. Baumann, Ueber gepaarte scwefelsauren im organismus, Pflugers Arch., Bd. 13, 1876, s. 287.

Bibliography.

24. Munk, zur Kenntniss d. Phenolbildender Substanzim harn. Pfluger's Arch., Bd.12, 1876, S.142.

25. Schaffer; Ueber die Ausscheidung des dem Tierkorper zugefuhrten Phenols. Journal f. Prakt. Chemie. Bd., 18, S.282.

26. Lievin und Falkson; Deutsche Zeitschr. f. Chir. Bd. 13, S.380.

27. Hack; Ueber des Resprptions Vermogen Granulirender flachen Deutsche Zeitsch. f. Chir. Bd.13, S.266.

28. Wilk's Guy's Hospital Reports, 1877.

29. Baumann; Zur Kenntniss der Aromatische Substanzen des Tierkorpers. Zeitsch. f. Phys.Chem. Bd.1, 1877, S.60

30. Fortora; Sul Assorbiments dell acids fenico e metods per riconoscerb nei liquidi organi. Morgagui Napoli, XIX, 1877, 32-37; also London Med. Record, 1876, p.564. 1877,p.455.

31. Baumann E.: Ueber die Bestimmung der Schwefelsaure im Harn. Zeitsch. f. Phys.Chem. Bd.1, 1877, S.70-71.

32. Baumann E.: Ueber gepaorte Schwefelsauren im Harn, Du Bois, Arch. 1877, S.576

33. Baumann u Herber, Ueber die Synthese von Aetherschwefelsauren und das verhalten einiger Aromatischen Substanzen im Tierkorper, Zeitsch. f. Phys. Chem., Bd.1, 1877, S.247; also Du Bois Archiv. f. Anat. u Phys., 1879, S.245.

34. Nothnagel - Rossbach, arzneimittellehre, 1878, S.458.

35. Christiani u.Baumann: Ueber den Art der Bildung des Phenolschwefelsaure in Tierkorper. Zeitsch f. Phys. Chem. Bd.2, 1878, S.350.

36. Tauber; Beitrage zur Kenntniss uber des verhalten des Phenols im Tierischen Organisms, Zeitsch. f. Phys.Chem. bd.2, 1878-9, S.366-71.

Bibliography.

37. Salkowski. Ueber die Pathologische Phenolausscheidung, Centralblat. f.d. Wissenschaften Bd.16, 1878. S.563, 753.

38. Christiani; Ueber das Verhalten des Phenols im Tierkorper, Zeitsch. f. Phys.Chem. Bd.2, 1878, S.273_287.

39. Langenbuch: Klinischer Beitrage zur Lehre von der Carbolintoxicationen. Berliner Klin. Wochenschr. Bd.28, 1878, S.412.

40. Kuster: Die Giftigen eigenschaften der Carbolsaure bei Chirurgischer Verwendung., Arch. f. Klin. Chir. Bd.23, 1878-9, S.117-155.

41. L. Brieger: Ueber Plenolausscheidung bei Krankheiten und nach Pyrosin gebrauch. Zeitsch. F. Phys. Chem. Bd·2. 1878, S.241; Hoppe-Seyler, Ibid., Bd.3, 1879, S.348

42. Jonge; Weitere Beitrage uber das Varhalten des Phenols im Tierkorper. Zeitsch f. Phys. Chem., Bd.3, 1879. S.119.

43. Baumann E; u Brieger L.Ueber, die Entstelung von Kresolen bei der foulniss , Zeitsch f. Phys. Chenne Bd.3, 1879, S.149; and Ber. der Deutsch Chein. Gesel. Bd.12, 1879. S.804.

44. Baumann; u.Presisse, Zur Kenntniss der Oxydayisnen und Synthesen im Tierkorper, Zeitsch f. Phys. Chem. Bd.3, 1879. S.156.

45. L.Brieger; Zur Kenntniss des Physiologishchen Verhaltens des Brenzkatechin und Hydrochinon und ihrer entstelung im Tierkorper, Du Bois Arch., 1879. Supplem.S.61.

46 L. Brieger; Ueber Phenolausschiedung by 'Krankheiten Zeitsch.f.Phys.Chem. Bd.2. 1878-9, S.241.

47. Baumann u. Preusse, Ueber die dunkele Farbe des "Carbolharns". Arch.f.Phys., Leipsig, 1879, S.245 - 249.

48. Billroth: Karbol Intoxicationen, Wien Med.Presse. Bd.20, 1879, 1881, 1883, also S.912.

Bibliography.

49. L.Brieger: Ueber die Aromatoschen produkte der Faulniss aus Eiweiss, Zeitsch. f. Phys.Chem., Bd.3, 1879, S.134 to 148.

50. Billroth: Chirurgische Klinik, Wien 1871-6, Berlin. 1879, S.39-53.

51. Sonnenburg: Zur diagnose und Therapie der Carbolintoxicationen. Deutsche Zeitsch. f. Chir. Bd.9, 1878, S.356 to 364; also Zur Lehre der Carbolintoxicationen, Centralblat. f. Chir., Bd.5, 1878. S.753; 785.

52. Kicklin, E. De l' intoxication Pheniquee et en particulier des accidents d'intoxication consecutifs a l'emploi de l'acide Phenique dans la pratique Chirurgicale. Gaz.Med. de Paris, 6 s.I, 1879, 345, 398, 423.

1880 - 1889.

53. L.Brieger; Ueber die fluchtigen Phenole, deren Aetherschwefelsauren im Menschlichen Urin-vorkommen, Zeitsch. f. Phys.Chem., Bd.4, 1880, S.204-208.

54. Nencki und Giacosa, Ueber die Oxydation der Aromatischen Kohlenwasserstoffe im Tier-korper. Zeitsch f. Phys.Chem. Bd.4, 1880, S.336.

55. E.Baumann und C.Preusse: Zur Geschichte der Oxydationen im Tierkorper, Zeitsch. f. Phys. Chem., Bd.4, 1880, S.455-458.

56. V.V.Bruns: Fort mit dem Spray! Berlin.Klin. Wochenschr. 1880, No.43.

57. Von Genser: Vergiften durch Carbolsaure nach ausserer anwendung, derselber bei einen 14 tage alten Kinde. Arch.f. Kinderh. Bd.1, 1880, S.459-465.

Bibliography.

58. Munk: Zur Kenntniss der Phenole im Harn, Arch. f. Anat. u. Phys. Chem., Supplement, 26, 1880.

59. Malmgren, J.A.: Poisoning from the External Use of Carbolic Acid. Eira Goteborg, IV., 1880, 432-435.

60. C. Paul: Systemic poisoning by the External Application of Carbolic Acid, Phila. Med. Times. X, 1879-80, p. 404.

61. Monti; Vergiftung durch Carbolsaure nach ausserer Anwendung derselben bei einem 6 wochen. Alten Kinde-Heilung, Arch. f. Kinderh. III, 1881-2, S.17-28.

62. Schmiedebeg, Die Oxydationen in Tierkorper. Arch. f. Exper. Path. und Pharmak. Bd.14, 1881, S.306.

63. L. Brieger: Ueber Phenolausscheidung bei Krankheiten und nach Tyrosin gebrauch. Zeitsch. f. Klin. Med. Bd.3 1881, S.468.

64. Falkson: Beobachtungen und Untersuchungen, uber Carbol urin und Carbolintoxication bei der Listerschen Wundbehandlung. Arch. f. Klin. Chir. Bd.26, 1881, S.204.

65. Falkson: Zur frage uber den Werth der Farbe des Urins und der Sonnenburgsche Methode fur die beurtheilung der Karbolintoxication, Centralblat. f. Chir., Bd.8., 1881, S.529-531.

66. Wolfhugel und Knorre, Zu der Verschiedenen Wirksamkeit von Carbol-oel und Carbol-wasser. Mettheil, a.d. Kaiser, Gesundsheits Amte, Bd.1, 1881, S.352.

67. E. Baumann; Ueber den Nachweis und die dorstellung von Phenolen aus dem Harn., Zeitsch. f. Phys. Chem. Bd.6, 1882, S.183.

68. E. Kulz: Zur Kenntniss der Synthetischen Vorgange im Tierschen Organismus, Arch. f. d. ges. Physiol. Bd.30, 1882-3, S.474.

69. Salkowski: Ueber die Quantative Bestimmung der Schwefelsaure und Aetherschwefelsaure im Harn. Zeitsch. f. Phys. Chem., Bd.10, 1886, S.346.

Bibliography.

70. Von Maschka: Todeines Kindes b'ald nach der Geburf. in folge Ausserer anwendung einer concentriten Losang, Vet Gschr. f. gerichte med. n.f. XLV, 1886, S.239-242.

71. Zwaerdemaker: Idiosyncrasie by Carbol-vergifting, Nederl. Tyoschr. v. Geneesk. XXII, 2 d., 1887, bl. 41-48.

72. F.Muller: Ueber Schwefelwasserstoff in Harn, Berlin Klin. Wochenschr., Bd.24, 1887, S.405, 436; also Ueber das Verhalten des Faces und der Producte der Darmfaulniss im Harn, ibid. S.433-435.

73. Bulikinsky: Hoppe-Seyler's Med. Chem. Untersuchungen. Heft 2, 1887, S.243.,

74. Simon: Poisoning in a child 22 months, by the Use of Carbolised Cotton Wool, London Medical Record, Oct.15, 1887. p.465.

75. Russo: Ueber Phenolausscheidung bei Krankheiten. Centralbalt. f. Klin. Medicin. Bd.10, 1888, S.306.

76. Wood: Therapeutics, Its Principles & Practice. 1888, p.594.

77. J. Messinger u. G. Vortmann; Bestimmung des Phenols in Harn, Ber. d. Chem. Gesch. Bd.22, 1889, S.2313; Sowie, Bd.23, 1890, S.2753.

1890-1899.

78. Mazzenga, Sull eliminazione del fenelo per le urine e sul rapporto fra la Medesima e quella dell'acid solforico, Progressor Med. Napoli, IV, 1890, 334-345, 434-479.

79. Warfield: Ueber Carbolgangren. Therapeut. Monat-shefte, 4, 1890, S.364.

80. Kellock, J.D. Carbolic Acid Gangrene, Med. News, Philadelphia. LVI, 1890, p.519.

Bibliography.

81. Kulz: Ueber einige gepaorte Glycuronsauren. Zeitsch. f. Biol. N.F. Bd.9, 1890, S.247.

82. Rumpf: Untersuchungen uber die quantativen Bestimmung des Phenolkorper des menschlichen Harns, Zeitsch. f. Phys.Chem, Bd.16, 1892, S.220, 242.

83. Keimann: Gutochten betreffend fahrlassige Todhung durch Aussere Anwendung von Karbolsaure, Vetljrschr.f.Gerichte Med. 3 F., Bd.II, 1891, S.63-73.

84. Rosenblatt: Poisoning from Carbolic Dressing in a child 5 weeks old. Przegl. lek. Krakow, XXXI, 1892, 359-361.

85. Frankenburger: Ueber Carbolgangren. Inaugural-Dissertation zur Erlangenig, 8th Dec. 1890, also Buffalo Med. & Surg. Journal, Oct.1982.

86. R.von Jaksch: Klinische diagnostik, 3 anfl. 1892.

87. Penny und Kossler: Ueber die Maasanalytische Bestimmung der Phenole im Harn, Zeitsch.f. Phys.Chem., Bd.17, 1893, S.117.

88. Arlois Strasser: Ueber die Phenol Ausscheidung bei Krankheiten, Bd.24, 1894., S.543.

89. Adams: Rapid Absorption of Carbolic Acid by an Eczematous skin. Arch. Pediat. N.Y.XI, 1894, p.825-827.

90. Eulenberg: Real Encyclopadie der gezammten Heil-kunde, 3, 1894, S.260.

91. S.Tauber: Die Wirkung der Schwefelsauren und der Schwefligsauren salze, sowie anderer Schwefelverbindungen bei Phenolvergiftung. Arch.f. Experm. Path. u. Pharmak. Bd.36, 1895, S.197-211.

92. Lucas & Lane: Two cases of Carbolic Acid Coma, Induced by the application of Carbolic Compresses to the skin. Lancet I, 1895, p.1361.

Bibliography.

93. Leusser: Ueber Carbolgangran. Munch. Med. Wochenschr. Bd. 43, 1896, S.338. Further literature given here.

94. Cohn: Todeines weinige Tage alten Kindes durch die Aussere Anwendung von Carbolsaure. Viertljhrs. f.Gerichte Med. Berlin., 3 F. XI, 1896, S.307.

95. Nothnagel: Die vergiftungen von Jaksch, Specielle pathologie und therapeut., Bd.1, 1897, S.340-6.

96. Lucas: A Case of Carbolic Poisoning from the Application of a Carbolic Compress to the skin. Lancet, II, 1897, p.204.

97. Binz: Lectures on Pharmacology, Vol.II, 1897, p.204.